MORPHINE EQUIVALENT DAILY DOSE POLICIES IN THE UNITED STATES: VARIATIONS IN STRUCTURE AND IMPACT ON PRESCRIBED DOSE

By Sara Heins

A dissertation submitted to Johns Hopkins University in conformity with the requirements for the degree of Doctor of Philosophy

Baltimore, MD
May, 2018

Abstract

Background: Prescription opioids are powerful painkillers that are highly addictive and may result in death when taken at high doses or combined with alcohol or other drugs. A major risk factor for prescription opioid mortality is high dose prescribing, leading many state level organizations to adopt policies intended to discourage prescribing above a certain standardized dose, known as a Morphine Equivalent Daily Dose (MEDD) threshold. The values of these thresholds vary significantly by the states and organizations that set them, and are used in different types of policies to influence prescribing behavior. Despite the proliferation of these policies in recent years, little is known about the variability in these policies or their impact on prescribed dose. The objectives of this dissertation are to systematically identify and characterize state-level MEDD threshold policies and evaluate the impact of a subset of these policies on prescribed dose in workers' compensation and privately insured populations.

Methods: State-level MEDD threshold policies were systematically reviewed and verified against existing policy compilations and academic literature. For states where no policies were identified, at least one representative of a state health agency was contacted to confirm the absence of any MEDD threshold policy. Policies were independently double coded on the categories: state, agency/organization, policy type, effective date, threshold level, and policy exceptions. Next, two workers' compensation guidelines identified in the review were evaluated using workers' compensation claims data from a large, national insurer. Policies from nine additional states comprised of guidelines, rules/regulations, legislative acts, and passive alert systems were evaluated using a large, national sample of commercial claims data. For both claims analyses, an interrupted time series with comparison states design was utilized with average monthly MEDD as the primary outcome. Additional stratified analyses examined each

state policy individually and evaluated the policies separately by groups explicitly excluded by the policies (e.g., patients with cancer, acute pain diagnoses, or receiving end of life care) to determine if the policies were being targeted as intended.

Results: As of June 2017, 22 states had at least one type of MEDD threshold policy, most commonly guidelines followed by prior authorization requirements, rules/regulations, legislative acts, claim denials, and alert system/automatic patient report. There was a wide range of threshold values (30-300 mg MEDD) with threshold levels generally decreasing over time. Most policies exclude some groups of opioid users, most commonly patients with terminal illnesses or acute pain. In the two states that passed workers' compensation guidelines, guideline passage was associated with a 9.26 mg decrease in prescribed MEDD and larger decreases were observed in claimants with chronic, non-cancer pain. In the nine states which passed MEDD policies aimed at the general population, results were more mixed. Policies were associated with 15% lower odds of any opioid use, but no significant change in the odds of receiving high dose prescriptions, specifically and there was actually a slight increase in prescribed dose when the population was restricted to opioid users. Furthermore, changes in opioid use did not appear to be targeted towards intended groups of patients.

Conclusions: This study finds that states have implemented a wide variety of MEDD threshold policies and there is little consensus as to threshold level or policy structure. In the context of a workers' compensation population, passage of MEDD threshold guidelines was associated with a decrease in prescribed MEDD. However, MEDD threshold policies were not associated with a decrease in prescribed MEDD in a privately insured population. It is possible that guidelines targeted towards a specific population, e.g., injured workers, may be more effective than those

aimed at the general population. Future work should examine the impact of MEDD threshold policies in other contexts, including impacts on patient health.

Thesis Readers

Dr. Andrea Gielen (Chair)

Dr. Caleb Alexander

Dr. Colleen Barry

Dr. Renan Castillo (Advisor)

Dr. Keshia Pollack

Dr. Eric Strain (Alternate)

Acknowledgments

As I come to the end of my doctoral program, I would like to take the time to thank the many individuals who have supported me and made this dissertation possible. Thank you to my advisor and mentor, Renan Castillo, for supporting me personally, academically, and professionally and helping me develop into the researcher I am today. Renan has always advocated for me, introduced me to new ideas and ways of thinking, and encouraged me to pursue research questions that excited me.

I am very fortunate to have spent the past seven years at Johns Hopkins, first as a research assistant and programmer, and then as a doctoral student. After seven years, I am still in awe of the amazing opportunities available to members of the Hopkins community and the amount of expertise concentrated in one place. I can't think of a better place to have grown as a scholar and researcher in the field of public health.

I would like to thank my committee members, Colleen Barry, Keshia Pollack, Caleb Alexander, Dorianne Feldman, Andrea Gielen, for their thoughtful feedback and guidance throughout the dissertation process. They have challenged me to consider different ways of looking at my research question, population, and analyses. I also received helpful advice from Dr. Lauren Nicholas on analytic methods, support from Albert Wu and Gerard Anderson in obtaining data, and technical support from Irene Murimi, Matthew Daubresse, and Mark Miller. Katherine Frey graciously served as an independent coder for the policies in Chapter 2 and provided valuable feedback on the manuscript.

Thank you to Adrienne Ghorashi, Lindsay Cloud, and The Policy Surveillance Project at Temple University, who assisted me with quality assurance and dissemination efforts for my second thesis chapter. Thank you to American International Group and Truven Health Analytics

for providing the data and user support for the third and fourth chapters of my study, respectively.

I would also like to thank the National Institute for Occupational Safety and Health (NIOSH) and the Department of Health Policy and Management at Johns Hopkins for funding my training and to the Agency for Healthcare Research and Quality (AHRQ) for funding my dissertation research. I am greatly indebted to Keshia Pollack for recommending me for the NIOSH training grant and to Renan Castillo, Colleen Barry, Caleb Alexander, Keshia Pollack, and Albert Wu for supporting my AHRQ grant application.

Last but certainly not least, I would like to thank my wonderful family and friends for all of their support throughout my doctoral program. My husband, Patrick Nadeau, who made sure that I kept my sanity while deep in the dissertation process, my son, Samuel, who has filled this past year with joy and purpose, and my parents Charlene Polio and Bill Heins, for always believing in my capabilities and encouraging me along the way. Thank you to my fellow cohort mates, especially Caroline Hanson, Shawn Du, and Dolapo Fakeye, for helping me survive Biostatistics our first year and for challenging me to be a better scholar. Thank you to my Baltimore crew, Andy and Austin Janitis, Eric Zatcoff, Joe Shemar, Bobby Angelo, Ariel Grossman, Geoff Winkley, and Renee and Alex Wisely for reminding me there is a life outside graduate school and getting me across the finish line.

Table of Contents

List of Tables

Chapter 4 Appendix

List of Figures

Chapter 1. Introduction

Nature and Burden of Prescription Opioid Morbidity and Mortality

Opioid analgesics are powerful painkillers and an essential tool for managing patients' pain. However, prescription opioids are also highly addictive and potentially fatal at high doses or when used in conjunction with alcohol or other drugs.[1] While the past fifteen years have seen a marked decrease in motor vehicle deaths and homicides[2] the number of overdose deaths from prescription opioids in the United States has doubled from 2002-2016.[3] Overall, there were over 14,000 deaths involving prescription opioids in 2016,[3] or roughly 40 deaths per day. Over one million people went to the emergency room due to prescription opioid misuse in 2011[4] and over ten million Americans reported nonmedical use (use in a manner not intended by the prescriber) of prescription opioids in 2014.[5]

Opioid overdoses are considered a type of poisoning injury and can be categorized as intentional (as a method of suicide) or unintentional. Although it is often difficult to ascertain whether a prescription drug overdose was intentional or unintentional, it is estimated that the rate of unintentional overdose of prescription opioids is approximately eight times the rate of intentional overdose.[6] Unintentional injury is the leading cause of death for all age-groups 1-44 and suicide is the second leading cause of death for ages 15-34.[7] Among unintentional injury deaths, poisoning is the leading cause of death, surpassing even motor vehicle deaths in recent years.[8] Opioid analgesics are less commonly used as a means for suicide, but are still of concern given their widespread availability.[6] The most common types of painkillers involved in overdose fatalities are buprenorphine, fentanyl, hydromorphone, methadone, and oxycodone.[9] While prescription opioids were the largest mortality contributor to the opioid epidemic until 2014, in

recent years, deaths from prescription opioids have been surpassed by the illicit opioid, heroin, and fentanyl, which can be used medically but is increasingly being illegally manufactured and sold.[3]

Social and Political Context

Prescription opioid abuse as a public health issue has a long and complex history. While, the issue of prescription opioid abuse has gained considerable attention in recent years, the problem is far from novel. Opioids, derived from the poppy plant, have been used to treat pain for thousands of years; they were thought to have been first used by the Sumerians around 3400 BC.[10] Morphine, which is still commonly used today, was developed in 1803 and a number of natural, semisynthetic, and synthetic opioid medications have been since developed.[10] Since that time, there has been considerable tension between the recognized medical use of opioids to treat pain and the serious problems of addiction, overdose, and recreational use.[10] The use of opioids in medicine grew during the 1800s, but with it grew the realization that opiates were physically addictive and could easily be abused.[10] In the late 1800s and early 1900s, there were considerable international efforts to curb the improper use of opioids including development of therapies for the treatment of opioid addiction, stricter prescribing standards, and creation of new, less addictive formulations.[11] In general, there was a growing sentiment that those with a history of substance abuse or addiction should not receive opioids, even following injury. However, in the late 1990s in the United States, views on pain management began to again change. Pain came to be known as "the fifth vital sign," meaning that clinicians were expected to routinely take pain ratings and include pain management as part of comprehensive treatment.[12] There was also a growing recognition that a substantial proportion of patients were not receiving

adequate pain treatment.[12] Research showed that pain was not only a symptom, but also had an independent effect on physical function and was worthy of treatment in and of itself.[13,14] Prescriptions of opioid analgesics for pain relief rose steadily along with prescription opioid-related mortality.[19]

As mortality from prescription opioids has increased in recent years, the view that the prescription opioid epidemic should be a top public health priority, has gradually gained acceptance. While drug overdoses, in general, were previously seen as belonging to the domain of law enforcement, the increase in the proportion of drug overdoses involving prescription drugs has led more people to view the issue as a matter of public health.[15] Furthermore, there has been a greater realization that drug addiction is not just about the actions of an individual, but rather involves a complex interplay between the individual, the drugs, and the environment. Prescription opioid addiction and overdose deaths are also increasingly being viewed as iatrogenic issues, giving the medical establishment a stronger moral imperative and increased agency to act.[16]

Epidemiology of Prescription Opioid Morbidity and Mortality

The burden of the opioid epidemic is felt across age, race, gender, and socioeconomic status and each group faces a unique set of challenges. However, some groups have an especially high risk of morbidity and mortality. Opioid use and overdose differ by gender, but this relationship is complex. Females generally report greater pain sensitivity[17] and more frequent occurrence of psychological distress,[18] both of which are risk factors for prescription opioid misuse.[1] Doctor-shopping, a practice in which patients visit multiple doctors in order to receive more opioid

prescriptions, is also more common among women.[1] Despite these relationships to several key risk factors, overall, males are at greater risk of misusing prescription opioids and have higher prescription opioid-related mortality, perhaps due to more frequent concurrent use of other drugs and alcohol.[10] Age has a similarly complex relationship. Overall, older patients are more likely to receive opioids, tend to receive higher doses, and are more likely to receive overlapping prescriptions;[19,20] however, younger individuals are more likely to use opioids nonmedically than older patients.[21] Perhaps for this reason, those in middle age groups (35-54) tend to have the highest levels of prescription opioid mortality.[22] Individuals who abuse alcohol and/or non-opioid drugs, are white, and have a low income are also at an increased risk of opioid misuse, overdose, and mortality.[10] Studies have suggested that residents of rural areas have higher rates of opioid related overdoses[1,23] and nonmedical opioid use[24] as compared to those in urban and suburban areas, but have fewer available addiction treatment resources.[25,26]

Opioid Morbidity and Mortality among Chronic Pain Patients and Injured Workers

Two populations of particular interest to researchers and policymakers are chronic pain patients and injured workers, both of whom are exposed to opioids through medical use. Individuals may experience chronic pain for a variety of reasons including previous traumatic injury, repetitive use injuries, or from complications of chronic conditions. Among chronic pain patients with long-term use of prescription opioids, psychiatric comorbidities and substance use disorders are extremely prevalent.[27] Although the relationship between chronic pain, substance use, and

psychiatric comorbidities is complex, there is some evidence of reciprocal relationships between these domains.[28,29]

Occupational health researchers and insurers have also become increasingly interested in prescription opioid addiction. Workers often initiate opioid use following an occupational injury and development of opioid addiction may delay return to work.[30,31] Previous research has found opioid use to be very common in injured workers with around one-third of shoulder and back injuries receiving opioids and nearly half of those patients going on to become long-term opioid users (>3 months of continuous use).[32] Furthermore, research suggests that opioid users in the workers' compensation population are more likely to receive high doses and to become long-term users than are opioid users in the general population.[33] Injured workers generally receive medical care paid for by workers' compensation claims, which can be a valuable source of information for researchers studying opioid prescribing practices in this population.

Current Policies Addressing the Opioid Epidemic

In response to the opioid epidemic, a number of initiatives have been undertaken at the local, state, and national levels. Prescription drug monitoring programs (PDMPs) are one such type of initiative enacted at the state level. PDMPs collect prescribing data in order to combat doctor shopping (visiting several different doctors to obtain a large volume of opioids without arousing suspicion).[34] Currently every state has an operational PDMP or has enacted legislation for its provision.[35] All state PDMPs collect data on the prescriptions filled by pharmacists, but beyond this shared central component, the functions and practices of state PDMPs vary greatly.[35] For example, some states also collect information on prescriptions written by doctors, flag patients

who purchase opioids with cash, collect information on different schedules, and share data with neighboring states.[35] All existing state PDMPs were created through legislation at the state level and most major differences in the overall structures of state PDMPs are outlined in these laws; however, regulation also plays an important role in PDMPs. The legislative acts which created the PDMPs designate their housing within different state agencies broadly categorized as Pharmacy Board/Licensing, Health and Human Services/Substance Abuse, or Law Enforcement.[35] These agencies have some leeway to regulate PDMPs without having to pass new laws. For example, in 2014, Massachusetts updated its regulations to collect data on a broader range of drugs, mandate a greater frequency of reporting, and allow for automatic reporting to doctors.[36] This regulatory authority, coupled with state-level implementation, gives states the ability to test potentially beneficial changes to PDMPs and the flexibility to adopt promising practices more quickly than they would be able to through legislative acts.

Other interventions to prevent prescription opioid overdose include automatic alerts within electronic health records (EHR) to indicate that a patient exhibits signs of nonmedical opioid use, safe opioid disposal programs, drug testing prior to opioid prescribing, and increased availability of opioid overdose rescue drugs such as Naloxone.[37] Substantial effort has also been expended creating formulations of opioids that have lower risk of addiction and are more difficult to abuse.[38–41] Despite these multi-pronged efforts to combat prescription opioid overdose, mortality has remained stubbornly high. After a small decrease in prescription opioid mortality from 2011 to 2012, deaths increased again every year from 2013 to 2016.[3] In general, there is only weak evidence supporting many of these interventions. A recent systematic review of seven types of interventions (PDMPs, insurer restrictions on prescribing, state-level legislation, guidelines,

naloxone, safe disposal programs, and education programs) found only weak to moderate evidence in support of the evaluated interventions.[42] In particular, the authors noted that no evaluations of state-level legislation and few evaluations of guidelines used comparison groups. Furthermore, little was done to differentiate between the effects of multiple interventions implemented simultaneously. Of the seven types of interventions evaluated, only provider and patient education programs had moderate evidence of an effect on patient outcomes, and these changes were generally only observed in the short-term.

Morphine Equivalent Daily Dose Thresholds

One commonly promoted component of programs to address the prescription opioid overdose epidemic is the establishment of MEDD thresholds. MEDD, also sometimes referred to as daily Milligrams Morphine Equivalent (MME), is a measurement that converts opioid prescriptions to their equivalent dose in morphine and divides the total prescription by days supply of the medication.[43] This measurement allows for comparison among different types of opioid formulations and strengths. The values of these thresholds vary widely by the states and organizations that set them and are used in different ways to regulate prescribing practices. Organizations that use MEDD thresholds include state Medicaid agencies, health departments, PDMPs and medical boards, Medicare, private health insurers, EHR administrators, and the Veteran's Administration (VA).[44–46] Occupational health organizations such as the American College of Occupational and Environmental Medicine (ACOEM),[47] the Official Disability Guidelines (ODG),[48] and state workers compensation boards[49–51] have also developed or adopted thresholds. Recently, the Centers for Disease Control (CDC) released their own MEDD threshold guidelines as part of a comprehensive strategy for combatting opioid use.[52]

Despite the proliferation of MEDD threshold policies in recent years, little work has been done to characterize or evaluate them. MEDD thresholds have been determined almost exclusively by expert opinion or adapted from other states and are generally not informed by clinical trials or observational studies. Evaluations of the effect of MEDD threshold policies have been limited to Washington State. Washington uses a different threshold than many other states and organizations and is not representative of populations elsewhere in the country, necessitating research into MEDD threshold policies in other contexts. Furthermore, evaluations in Washington State have not included a comparison state or examined the differential effect of the policy in relevant clinical subgroups, such as cancer patients or individuals with terminal illnesses.

While setting MEDD thresholds may discourage high dose prescribing—an important risk factor for prescription opioid mortality—the use of MEDD thresholds is not without criticism. As a practical matter, while MEDD policies are generally intended to restrict total prescribed dose, prescribers may fail to take into account early prescription refills or opioid prescriptions from other sources when calculating the MEDD. Even when calculating MEDD for a single prescription, prescribers may still encounter issues. For example, in 2015, researchers sent a survey to pharmacists, physicians, nurse practitioners, and physicians assistants asking them to calculate the morphine equivalents for four different drugs using any resources available to them.[53] For each drug and among each provider group, their calculations had enormous variability. While a small number of policies provide mechanisms to automatically calculate MEDD and take into account multiple and overlapping prescriptions (e.g., states with alert

systems/automatic reports), most policies leave it to the provider to make these calculations. There is also a larger critique of MEDD as a measure, namely that it downplays important differences between different opioid formulations, particularly fentanyl and methadone.[53,54] Critics also argue that it is impossible to assign a single MEDD threshold level to all opioid users, regardless of body mass, condition, or individual tolerance levels.[53–55]

Objective, Specific Aims, and Hypotheses

Given the lack of evidence supporting MEDD threshold policies, there is a clear need for rigorous evaluation of existing policies. The overall goal of this research is to characterize existing state-level MEDD threshold policies in the United States and to evaluate the impact of a selection of these policies on prescribing practices in workers' compensation and privately insured populations. Specific aims of the research are as follows:

Aim 1. Systematically review and document existing MEDD threshold policies at the national, state, and local levels. The following product shall be created upon completion of this aim:

Product 1. A compendium of state-level MEDD threshold policies implemented in the United States. For each policy, information will be compiled about threshold value, date of implementation, policy exclusions, and date of implementation.

Aim 2. Determine the impact of state workers' compensation board policies identified in Aim 1 on prescribed dose using claims data from a large, national workers' compensation insurer 2010-2013. I hypothesize that:

Hypothesis 2.1. There will be an overall decrease in prescribed opioid dose in states with workers' compensation board MEDD threshold policies relative to states no such policies.

Hypothesis 2.2. Workers' compensation board MEDD policies will be associated with a greater decrease in MEDD among opioid users with chronic, non-cancer pain—the group primarily targeted by the policies—than among users with acute pain or cancer diagnoses.

Hypotheses 2.1 is consistent with the results of evaluations of MEDD threshold guidelines in Washington State.[56] To date, no study has looked at the impact of MEDD threshold policies in cancer and acute pain patients separately to determine if policies are being targeted as intended.

Aim 3. Determine the impact of state health department, medical board, PDMP, and legislative policies on prescribed opioid dose in a privately insured population. I hypothesize that:

Hypothesis 3.1. There will be a reduction in prescribed opioid dose in states with MEDD threshold policies from pre- to post-implementation periods relative to states without such policies.

Hypothesis 3.2. The passage of rules/regulations, legislative acts, and passive alert systems compared to the passage of guidelines, will be associated with larger decreases in MEDD prescribed opioid doses.

Hypothesis 3.1 is consistent with prior evaluations of MEDD threshold guidelines in Washington State,[56,57] in workers' compensation and Medicaid populations, respectively. However, it is unknown whether guidelines would have the same impact in privately insured populations, where insurers may not be able to exercise as significant influence. Similarly, other types of MEDD threshold policies, including rules/regulations, legislative acts, and passive alert systems, have not been evaluated. However, evaluations of prescribing policies in other contexts support the hypothesis that other types of policies may be more effective than guidelines in changing prescriber behavior. These studies have generally found that adherence to published

prescribing guidelines is low, even years after a guideline has been published.[58–61] However, passive alert systems—systems that notify providers of prescribing guidelines either through decision support within an EHR, by e-mail or through paper letters during or shortly after eligible patient encounters—tended to significantly improve provider adherence to prescribing guidelines, particularly when the alerts were timely and provided a recommended course of action.[58–60,62,63] One study which systematically reviewed several types of policy structures found that multimodal methods had stronger effects than single methods.[59]

Innovation

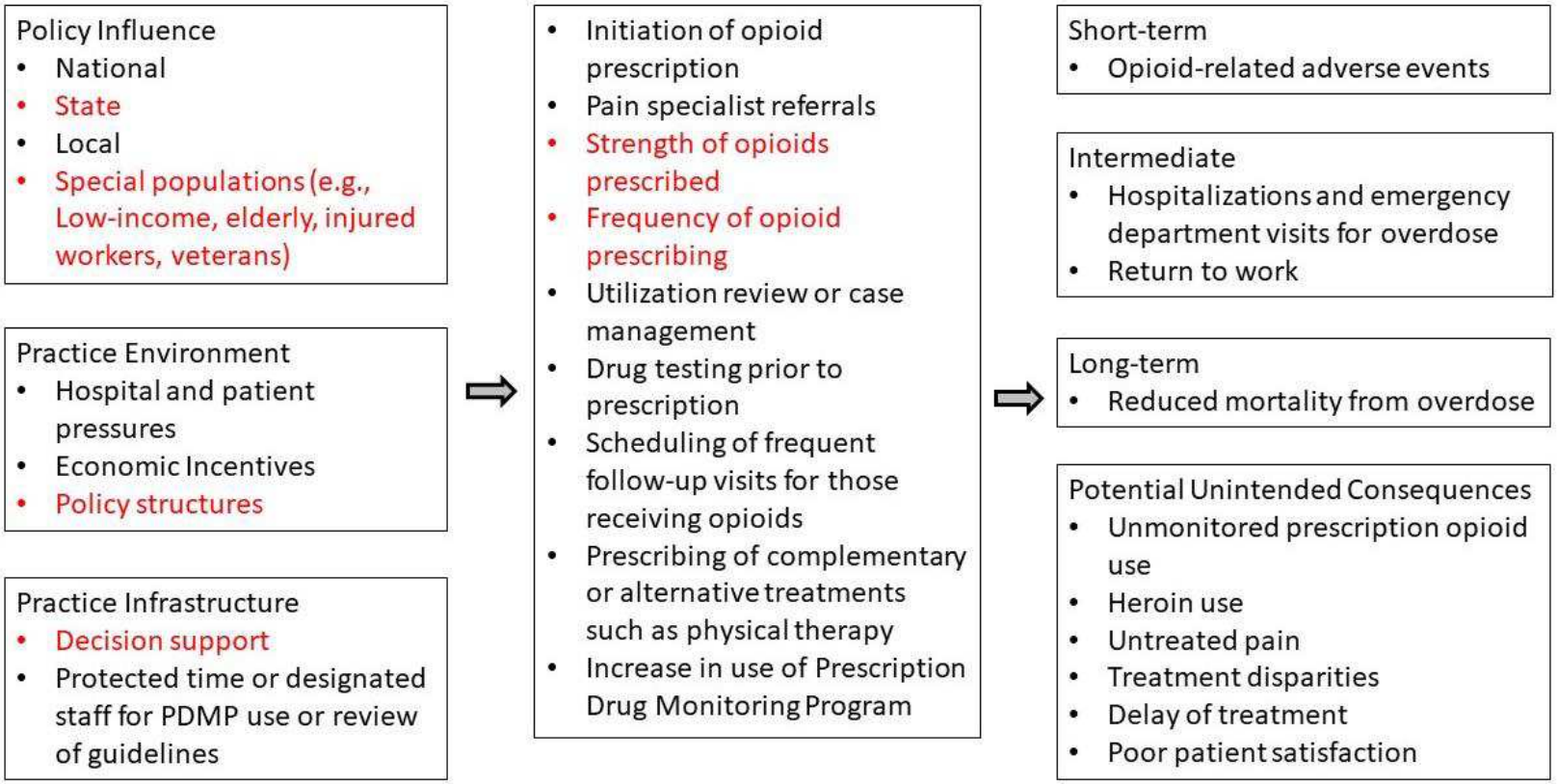
To date, no systematic documentation of MEDD threshold policies within the United States has been published. Existing reviews are not comprehensive and leave out critical information necessary to evaluate the effect of these policies. This compendium is a necessary first step to evaluations of MEDD threshold policies and will be an invaluable tool to researchers. A review that comprehensively documents threshold levels, date of implementation, means of measurement and enforcement, and means of dissemination is needed to set pre- and post- periods, select appropriate comparison states, and differentiate between specific and non-specific effects of the policies. Building off of the review of threshold levels, this project will then analyze the impact of a selection of state policies on prescriber behavior in workers' compensation and privately insured populations. This will be the first analysis of MEDD threshold policies outside of Washington State and the first evaluation that utilizes comparison states, strengthening the case for a causal relationship. Since Washington implemented their MEDD guideline, several state and national organizations have implemented their own policies with varying threshold levels and methods of enforcement and dissemination. Evaluations of

these policies can provide insight into which strategies have the biggest impact on prescribing practices and patient outcomes. These results can then provide guidance to organizations who are considering adopting or revising MEDD threshold policies.

Conceptual Framework

The Donabedian Quality of Care Model[64] is the guiding conceptual framework. The Donabedian model examines healthcare quality issues through a lens of structure, process, and outcome, with structures representing the resources, environment, and policies in place, process representing the actions of the medical establishment, and outcomes representing health outcomes experienced by patients. In this dissertation, Chapter 2 addresses structure, Chapters 3 and 4 addresses process, and future research addresses outcomes. Chapter 2 will define the structure of MEDD threshold policies and describe the "policy environment" faced by prescribers who work within certain states or with different patient groups. Chapters 3 and 4 will evaluate the impact of MEDD threshold guidelines on prescribers' processes of prescribing opioids in workers' compensation and private insurance populations, respectively. The primary measures of interest in Chapters 3 and 4 will be average MEDD, which is a function of the strength of the opioids prescribed, the volume of pills prescribed, and number of simultaneous prescriptions. Future work will evaluate the impact of MEDD threshold policies on patient outcomes: time to RTW and opioid overdose or adverse events. This framework is presented in Figure 1 with the specific structures and processes addressed highlighted in red. The other structures, processes, and outcomes are outside the scope of this dissertation, but will be considered in the interpretation of results and addressed in future work.

Figure 1. Conceptual model[a]



[a]Adapted from the Donabedian Quality of Care Model

Chapter 2. State-Level Morphine Equivalent Daily Dose Policies, 2007-2017

Introduction

Prescription opioid misuse is a significant problem which has gained considerable national attention in recent years. In particular, prescription opioid-related mortality has doubled in the United States between 2002 and 2016[65] prompting a flurry of recommendations and policies aimed at stemming the epidemic. While a robust literature exists detailing the epidemiology of prescription opioid misuse, there is a lack of consensus as to which policies are most effective at reducing mortality and improving patient outcomes.[42] Previous research indicates that patients who receive higher doses of prescription opioids have an increased risk of overdose and mortality relative to patients who receive lower doses.[66–68] Given this association, a commonly promoted tool to address the prescription opioid overdose epidemic is the establishment of Morphine Equivalent Daily Dose (MEDD) thresholds. MEDD, also sometimes referred to as daily Milligrams Morphine Equivalent (MME), is a measurement that converts opioid prescriptions to their equivalent dose in morphine and divides the total prescription by days supply (the number of days the prescription is intended to last).[43] This measurement allows comparison among different types of opioid formulations and strengths, and accounts for multiple prescriptions patients may simultaneously receive. The threshold levels and structures of these policies vary widely by the states and organizations that set them, and are used in different ways to regulate prescribing practices. The first MEDD threshold policy was in the form of an interagency guideline passed by Washington State in 2007, which set a "yellow flag" threshold of 120 MEDD based on the recommendation of a consensus panel of prescribers.[69] Since that time, a majority of states have implemented some type of MEDD policy, though evaluations of the policies have been limited to Washington State.[56,70,71]

The purpose of this article is to comprehensively describe the landscape of MEDD threshold policies at the state level. Currently, no comprehensive list of these policies exists. In this article, MEDD threshold policies refer to state-level guidelines, legislative acts, rules and regulations, criteria for claim denial or prior authorization, or passive alert systems which seek to reduce the MEDD prescribed to patients. Specific features of these policies are described and documented to lay the groundwork for future empirical evaluation of the effectiveness of MEDD threshold policies.

Methods

A systematic search of state-level MEDD threshold policies enacted from January 1, 2007 to June 1, 2017 was conducted. LexisNexis and Westlaw Next were used to conduct a comprehensive search of legislative acts in all 50 states and the District of Columbia using the terms "morphine equivalent," "milligrams morphine," "opioid dose threshold," and "opioid dose maximum." These same terms were also used to find non-legislative state-level policy documentation on Google. Additionally, each state Medicaid Agency, Health Department, Prescription Drug Monitoring Program, Workers' Compensation Board/Division, Medical Board, and Pharmacy Board website was checked to determine if any other MEDD threshold policies existed. The comprehensiveness of the list was validated in several ways. First, the list was checked against existing compilations of policies such as the Agency for Healthcare Research and Quality (AHRQ) guideline clearinghouse,[72] The Brandeis PDMP Center of Excellence's report on PDMPs with passive alert systems,[46] the National Alliance for Model State Drug Laws 2016 report on State Pain Management and Prescribing Policies,[73] and the University of Wisconsin Pain and Policy Studies Group's 2015 Report on Profiles of State Policies Governing

Drug Control and Medical Pharmacy Practice.[74] None of these compilations are comprehensive, cover the full range of policy types examined in this paper, or systematically code characteristics of the policies, but they do serve as useful checks on the completeness of the current study. The Medicaid policies were checked against the Medicaid Drug Utilization Review (DUR) Annual Report Survey,[75] which lists states with Medicaid agencies responding "yes" to the question, "Have you set recommended maximum morphine equivalent daily dose measures?" Second, the list was checked against academic literature using the above search terms, for references to MEDD threshold policies. Finally, for states with no MEDD threshold policy found, at least one representative from a state health agency was contacted to confirm the lack of a formal policy. The positions of these representatives varied based on publicly available contact information, but frequently included the state's PDMP administrator or a member of the state's Medicaid DUR Board. In some cases, the representative could not confirm the lack of a policy, but was able to refer me to another individual with more knowledge of policies in the state. State and national opioid policies which involved MEDD but did not meet all of the study's inclusion and exclusion criteria were collected and are listed in Appendix 1, but should not be considered comprehensive.

After the final list of MEDD threshold policies was completed, documentation for each policy was reviewed to define a list of variables for coding each policy. A second researcher independently coded each policy according to this list of variables and refined code definitions where needed. The final list of variables included state, the effective date of the policy, organization(s) that contributed to the policy, policy type, threshold level, patient groups excluded from the policy, whether or not short courses of opioids were excluded from the policy, and under what circumstances the threshold level may be exceeded. Policy type definitions are

defined in Table 1. Two researchers independently coded the first eight policies (alphabetically by state) and had a divergence rate of 33%. Divergent codes were discussed and resolved and clarifying edits were then made to the codebook based on divergent answers. The two researchers then independently coded the remaining policies with a divergence rate of 21% and repeated the process of resolving differences in coding and clarifying the codebook based on divergent answers. Divergent codes occurred most frequently for the categories "patient groups excluded from the policy" and "under what circumstances the threshold level may be exceeded." The full protocol and codebook are provided in Appendix 2.

Results

Between January 1, 2007 and June 1, 2017, 22 states (43% of all states) enacted 31 MEDD threshold policies (Table 2). The most common policy structure observed was guideline (13 states) followed by prior authorization (4 states), rule/regulation (4 states), legislative act (3 states), claim denial (2 states), and alert system/automatic patient report (2 states). A map of policy type by state is displayed in Figure 1.

The state-level agencies or organizations responsible for the policies were most frequently the state's medical board (9 states), workers' compensation board/agency (5 states), health department (5 states), legislature (3 states), pharmacy board (2 states), and PDMP (2 states) with some state policies being implemented by multiple agencies or organizations.

A majority of states explicitly excluded certain patient groups from their MEDD policies with the most common exceptions being for terminal/hospice/palliative care patients (12 states),

acute/etiologic pain patients (10 states), and cancer/malignant pain patients (8 states)(Table 2). A majority of states also had policies which specified circumstances under which MEDD thresholds could be exceeded or triggered recommended or required actions when a threshold was exceeded. Most commonly, these circumstances involved referral to a specialist (14 states), pain contract/patient education (7 states), clinical judgment (6 states), or improved pain or function (5 states). Five states made exceptions for short courses of opioids, defined as less than 90 days (4 states) or 4 days (1 state).

The first policy was in the form of a guideline implemented in 2007 by Washington State which recommended against prescribing above 120 MEDD. This guideline has served as a model for other states with a plurality of states (10) adopting the 120 MEDD threshold (Table 2).

Over the years, progressively lower thresholds have been introduced in state guidelines (Figure 2). Other types of potentially higher impact policies have also been introduced in more recent years. While it is difficult to comment on trends given the small number of each of these types of policies, it is notable that the two claim denial policies have the highest thresholds (300 MEDD) and there appears to be an overall trend of higher dose thresholds among more restrictive policy types, such as Legislative Acts, Claim Denial, and Prior Authorization. In general, early policies had higher thresholds that were broadly applied. More recent policies have lower thresholds and stricter enforcement mechanisms, but are more specific about who the policy is intended to cover.

A few states have enacted multiple policies (Figure 3). In some cases, states have moved from less restrictive to more restrictive policy types. For example, Colorado released a guideline in 2014, then implemented prior authorization and claim denial in 2016. Other states have had multiple organizations implement guidelines or have lowered their thresholds.

Discussion

MEDD threshold policies have proliferated over the past decade, but there is significant variation in these policies. Overall, there has been a trend away from guidelines to more restrictive policy types as well as a decrease in threshold level. Most policies explicitly acknowledge that MEDD threshold levels should not apply to certain patient groups or allow for circumstances under which thresholds may be exceeded.

It is important to note that the lack of a MEDD threshold policy should not be construed as a lax regulatory opioid environment for a state. Many types of prescription opioid policies exist and MEDD thresholds are only one way of influencing prescribing behavior. Some states with no MEDD threshold policy which meets this study's criteria have other types of opioid policies including Medicaid lock-in programs for opioid users,[76] formularies that require prior authorization for some or all types of opioids,[77] quantity limits for individual types of opioids,[78] or limits on days supply of opioids.[79] While none of these policies specifically sets a MEDD threshold, it is reasonable to expect that these types of policies may nonetheless lower the overall MEDD prescribed.

Conversely, it is also important to note that MEDD threshold policies may not always work as intended. While the MEDD policies included in this study are all intended to restrict total MEDD, prescribers may not take into account opioid prescriptions from other sources or early prescription refills when calculating the MEDD they are prescribing. On a more basic level, there is still a lack of understanding among providers on how MEDD is calculated. A 2015 study sent a survey to pharmacists, physicians, nurse practitioners, and physicians assistants asking them to calculate the morphine equivalents for four different drugs using any resources available to them.[53] For each drug and among each provider group, their calculations had enormous variability. While a small number of policies provide mechanisms to automatically calculate MEDD and take into account multiple and overlapping prescriptions (e.g., the two states with alert systems/automatic reports), most policies leave it to the provider to make these calculations.

Beyond the practical consideration of calculating MEDD, there is also a broader criticism of MEDD as a measure. Many researchers have argued that MEDD policies dangerously downplay important differences between different opioid formulations or fail to take into account individual differences in drug tolerance.[53–55]

In February of 2016, the Centers for Disease Control (CDC) implemented their own MEDD threshold guideline which stated that prescribers "should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day."[80] The guideline was well publicized and one might expect that, following the passage of this guideline, there would be less variation in MEDD threshold

level for new policies. However, this change did not appear to have a significant effect on state-level policies. Of the seven state-level policies enacted following the CDC guideline, threshold values varied widely (between 30 and 300), and only two of those states (Alaska and Wisconsin) set thresholds in line with CDC recommendations. The continued variation in policy may be due to the cautious language used by the CDC in endorsing a dose threshold or it may be that only states who did not agree with the CDC guidelines felt that it was necessary to implement their own policies. Further research on states' processes for setting threshold levels is necessary to understand why such variation has persisted.

In addition to processes by which states set thresholds, understanding a number of other policy characteristics not explored here may be of great interest and aid in the future evaluation of these policies. In particular, information about enforcement mechanisms was often lacking from the policy documentation. For example, Medical Board Rules are stated as imperatives, and, in theory, violating these rules may result in losing one's medical license. However, it is unclear how frequently this happens in practice. It is not clear that these states have any automated way of verifying these rules are followed and noncompliance may only be discovered among audits of high volume prescribers. Conversely, guidelines, which do not use imperative language, may nonetheless make big impacts on prescribing behavior. Guidelines can be used by individual insurers within a state to justify claim denial of high dose prescriptions or target high dose prescribers for utilization review. Understanding the nuanced mechanisms by which MEDD threshold policies influence provider behavior would require in-depth qualitative research that is beyond the scope of this manuscript, but is an important area for future research.

Public Health Implications

MEDD thresholds are a promising policy tool, but there is a lack of consensus as to how the thresholds should be used and what at what threshold level they should be set. Further research is needed to determine which types of policies are most effective and if they are targeting the patients most at-risk for overdose. Understanding the variation in MEDD threshold policies is an important first step in evaluation.

Tables

Table 1. Policy type definitions

Term	Definition
Guideline/recommendation	Provides a recommended threshold over which prescribers should not exceed or should only exceed if special precautions are taken. Guidelines/recommendations have no mechanism of enforcement.
Rules/regulations	Similar to guidelines, but are stated as an imperative (e.g., "must" "shall") and may or may not have an explicit means of enforcement.
Legislative Act	Any law passed by the state's legislative body which has gone into effect. Proposed bills that never became law are not included.
Alert System/Automatic Patient Report	A mechanism by which targeted, unsolicited letters or alerts sent either by mail or electronically and inform prescribers that patients under their care have exceeded a given MEDD threshold. Follow-up action may or may not be required.
Prior Authorization	A requirement that mandates prior approval from a third party before prescriptions above a given MEDD threshold may be filled.
Claim Denial	A mechanism by which a third party denies prescription fills above a given MEDD threshold. In cases where Prior Authorization documentation explicitly states that prescriptions above a given MEDD threshold will not be approved, Prior Authorization and Claim Denial may be coded as two distinct policies.

Table 2. Frequency of policy characteristics

	States, Number (%) N=22	Policies, Number (%) N=31
Type of Policy		
Guideline	13 (59%)	15 (48%)
Rule/Regulation	4 (18%)	4 (13%)
Prior Authorization	4 (18%)	4 (13%)
Legislative Act	3 (14%)	4 (13%)
Claim Denial	2 (9%)	2 (6%)
Alert System/Automatic Patient Report	2 (9%)	2 (6%)
Sponsoring Organization		
Medical Board	9 (41%)	9 (29%)
Medicaid	6 (27%)	7 (23%)
Workers' Compensation	5 (23%)	6 (19%)
Health Department	5 (23%)	5 (16%)
State Legislature	3 (14%)	4 (13%)
Pharmacy Board	2 (9%)	2 (6%)
PDMP	2 (9%)	2 (6%)
Threshold Level		
30	2 (9%)	2 (6%)
50	1 (5%)	1 (3%)
60	1 (5%)	1 (3%)
80	3 (14%)	4 (13%)
90	4 (18%)	4 (13%)
100	5 (23%)	5 (16%)
120	10 (45%)	11 (35%)
300	2 (9%)	2 (6%)
Patient exclusions		
Terminal/hospice/palliative care	12 (55%)	14 (45%)
Acute/etiologic pain	10 (45%)	10 (32%)
Cancer/malignant pain	8 (36%)	11 (35%)
Long-term care facility/nursing home	5 (23%)	5 (16%)
ER care patients	2 (9%)	2 (6%)
Other patient groups	3 (14%)	3 (10%)
No patient groups excluded	7 (32%)	7 (23%)
Short courses of opioids excluded	5 (23%)	5 (16%)
Excluded circumstances		
Specialist consulted	14 (64%)	15 (48%)
Pain contract/patient education	7 (32%)	7 (23%)
Clinical judgment	6 (27%)	7 (23%)
Improved pain or function	5 (23%)	5 (16%)
Evidence of tapering	4 (18%)	4 (13%)
PDMP checked	4 (18%)	4 (18%)
Drug testing	3 (14%)	3 (10%)
Other circumstances specified	3 (14%)	3 (10%)
No circumstances specified	9 (41%)	10 (32%)

Abbreviations: ER, Emergency Room; PDMP, Prescription Drug Monitoring Program

Figures

Figure 1. Policy type by state

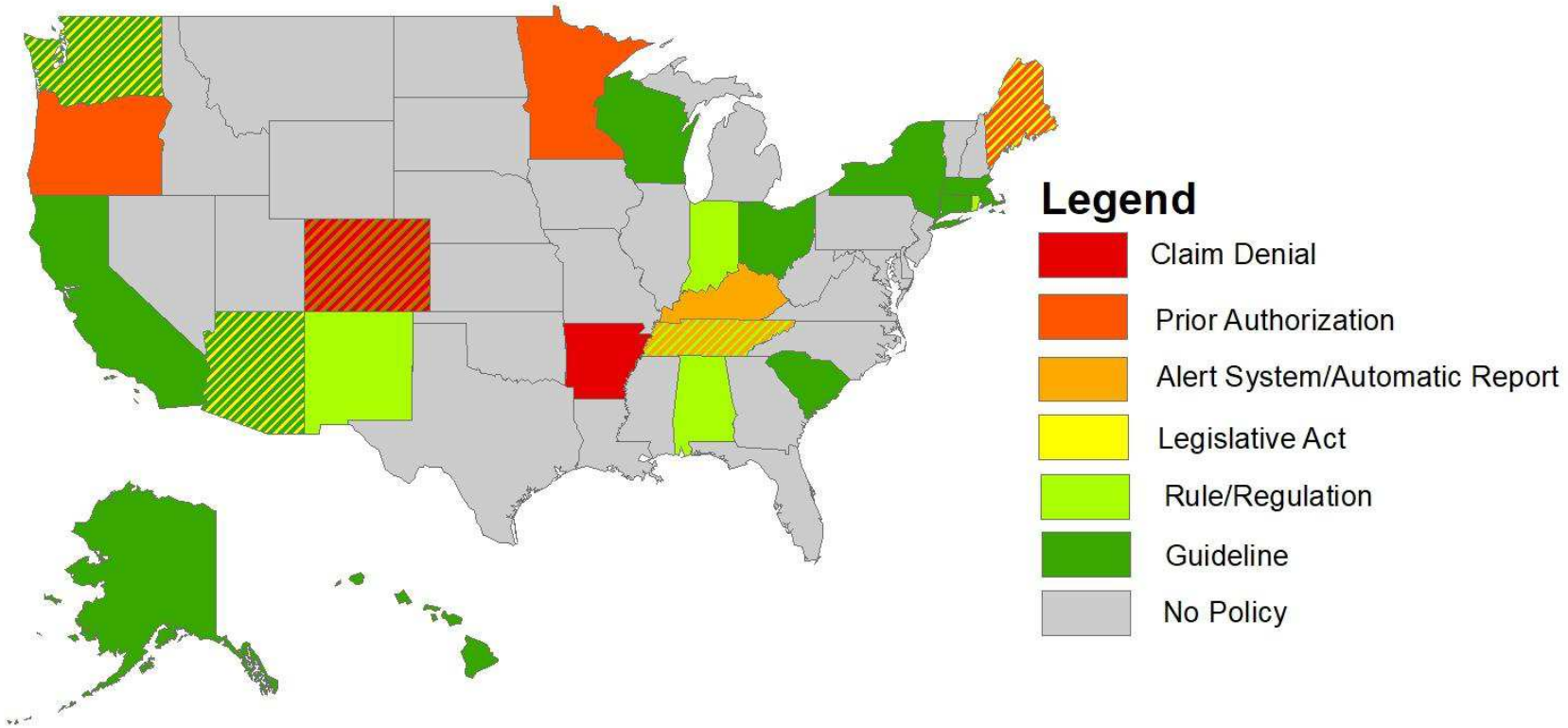


Figure 2. MEDD threshold level and type over time

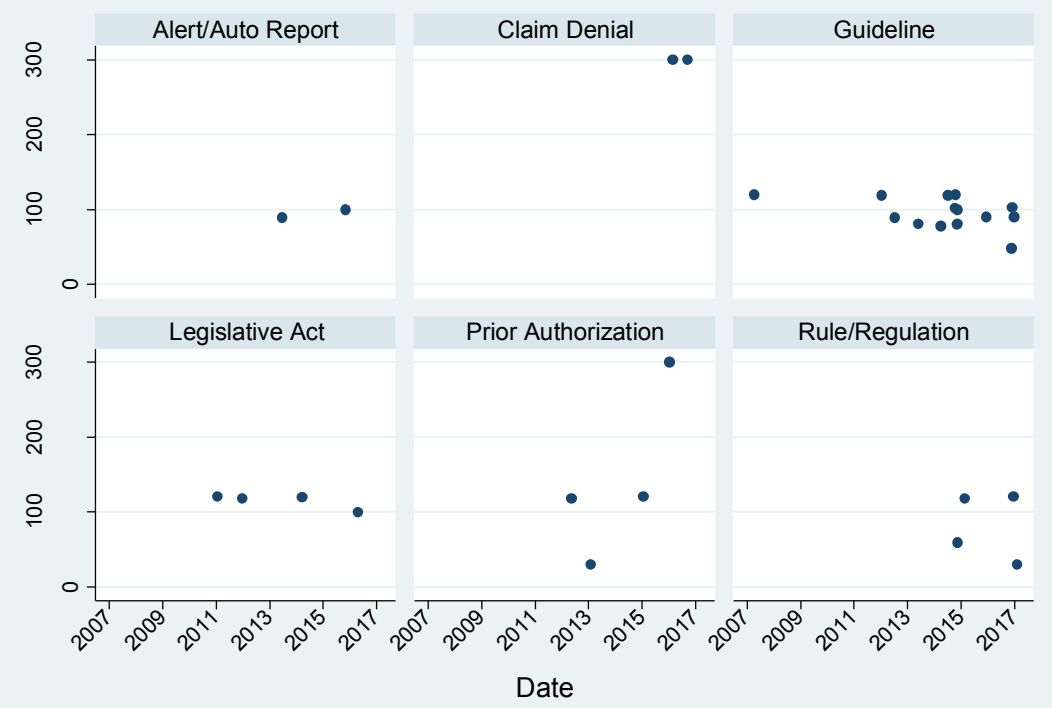
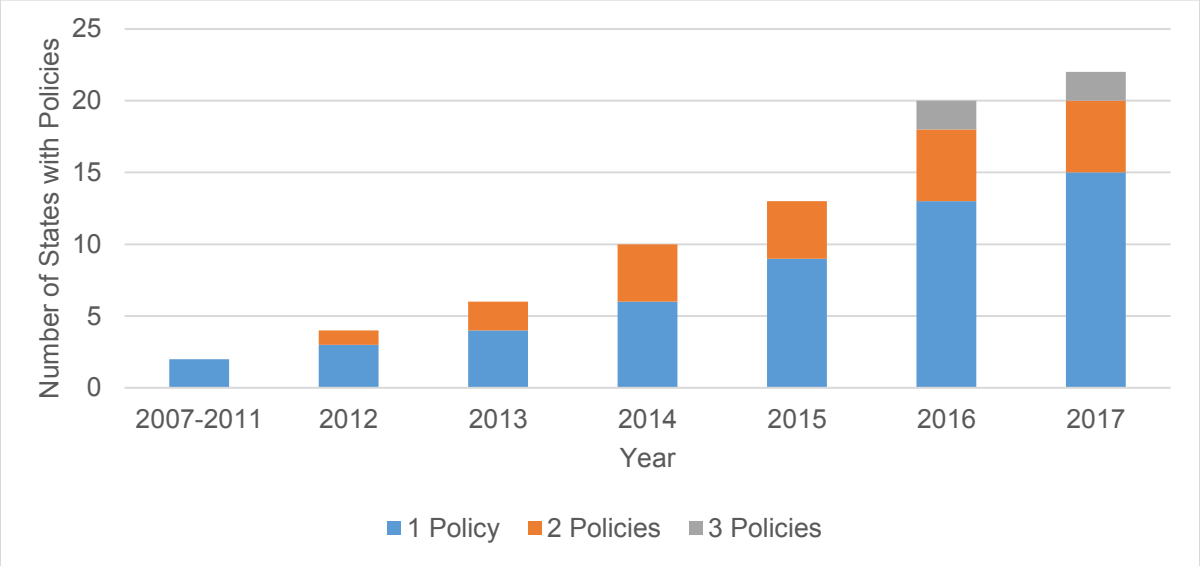


Figure 3. Number of states with MEDD policies over time



Appendix

Appendix 1. Relevant MEDD policies not meeting inclusion criteria

Citation: Alaska Medicaid. Prior Authorization Requirements Extended-Release/Long-acting Opioid Analgesics (all strengths). April 17, 2015. http://dhss.alaska.gov/dhcs/Documents/pharmacy/pdfs/Extended-Release-Opioids-PA_201504_APPROVED.pdf. Accessed November 30, 2017.

Policy Description**:** Establishes prior authorization for some types of opioids at any dose and quantity limits for some opioids.

Reason Not Included**:** MEDD criteria did not apply to all opioid drugs and there is no overall MEDD prior authorization criteria.

Citation: Health Options Highmark Blue Cross Blue Shield Delaware. Prior Authorization Conditions for High Dose Narcotics and Long and Short Acting Narcotics. January 2017. https://highmarkhealthoptions.com/sites/default/files/Narcotics.pdf. Accessed November 30, 2017.

Policy Description: Establishes quantity limits for long and short acting opioids.

Reason Not Included: MEDD threshold only applies to single Managed Care Organization in Delaware and is not a statewide Medicaid policy.

Citation: Georgia Composite Medical Board. Notice of Intent to Amend and Adopt Rules. https://medicalboard.georgia.gov/sites/medicalboard.georgia.gov/files/related_files/site_page/Rule%20360-3-.06%20Pain%20Management.pdf. Accessed November 30, 2017.

Policy Description: Doctors must follow-up with patients taking >30 MEDD at least every 3 months.

Reason Not Included: The policy only applies to Schedule II and III opioids and only recommends increased follow-up after exceeding a given MEDD with no other recommended course of action.

Citation: Electronic-Florida Online Reporting of Controlled Substances. 2015-2016 Prescription Drug Monitoring Program Annual Report. December 1, 2015. http://www.floridahealth.gov/statistics-and-data/e-forcse/_documents/2016PDMPAnnualReport.pdf. Accessed December 8, 2017.

Policy Description: E-FORCSE (Florida's PDMP) provides an overall MEDD calculation for providers when they login to the report.

Reason Not Included: Although MEDD calculations for providers when they login to the report, this calculation is not accompanied by any threshold recommendation or tied to any automatic alerts.

Citation: Opioid prescribing: A systematic review and critical appraisal of guidelines for chronic pain. Illinois Department of Healthcare and Family Services and UIC College of Pharmacy. 2014. https://www.illinois.gov/hfs/SiteCollectionDocuments/3opioidprescribing.pdf

Policy Description: The Illinois State Medicaid Agency reviewed and disseminated existing opioid prescribing guidelines including MEDD guidelines, but did not explicitly endorse any specific guideline.

Reason Not Included: This is a systematic review of existing guidelines rather than an endorsement of any guideline by an included state agency.

Citation: Board adds CDC guideline on opioid prescribing to list of resources for chronic pain treatment. Iowa Medical Board. 2016. http://www.medicalboard.iowa.gov/Board%20News/2016/Press%20release%20-%20Board%20adds%20CDC%20guideline%20on%20opioid%20prescribing%20to%20list%20of%20resources%20for%20physicians%20who%20treat%20chronic%20pain%20-%20%20August%2029%202016.pdf

Policy Description: A statement from the Iowa Board of Medicine which encourages physicians to consider the 2016 CDC opioid prescribing guidelines including MEDD thresholds.

Reason Not Included: This was considered a dissemination of existing CDC guidelines rather than guidelines sponsored by an included state-level organization.

Reference: Passport Health Kentucky Medicaid Prior Authorization Form. Passport Health Plan Kentucky Medicaid. http://passporthealthplan.com/wp-content/uploads/2017/01/Greater-Than-120-Morphine-Equivalent-Dose-MED-Edit.pdf

Policy Description: Requires prior authorization for opioid prescriptions above 120 MEDD.

Reason Not Included: Passport Health is one of Kentucky Medicaid's HMOs, but the prior authorization requirement does not apply to all Medicaid patients.

Reference: Memo on High Dose Limits. The Commonwealth of Massachusetts Executive Office of Health and Human Services Office of Medicaid. January 2016. http://www.mass.gov/eohhs/docs/masshealth/pharmacy/opioid-letter-high-dose-limits.pdf

Policy Description: Medicaid requires prior authorization for high doses of individual drugs above a certain MEDD threshold, but the threshold is drug dependent and there is no overall MEDD threshold in place.

Reference: Minnesota Revisor 5221.6110. Long-Term Treatment with Opioid Analgesic Medication. https://www.revisor.mn.gov/rules/?id=5221.6110
Policy Description: In workers' compensation patients, increased follow-up is recommended for opioid use above 120 MEDD.

Reason not Included: Does not meet the inclusion criteria "Policies which recommend increased follow-up after exceeding a given MEDD with no other recommended course of action were not included."

Reference: Provider Bulletin Express Scripts Physician Outreach Program-Morphine Equivalent Dose (MED). Montana State Fund. http://safemt.com/express-scripts-physician-outreach-program-morphine-equivalent-dose-med/

Policy Description: Providers with patients receiving opioids paid for by the Montana State Fund—Montana's state-funded workers' compensation insurer—will receive letters when individuals receive opioids in excess of 120 MEDD.

Reason Not Included: The Montana State Fund is only one workers' compensation insurer in Montana and injured workers not covered by the fund are not subject to these alerts.

Reference: Drug Utilization Review (DUR) Board Meeting. February 13, 2014. Mississippi Division of Medicaid. https://medicaid.ms.gov/wp-content/uploads/2014/04/DURMinutes021314.pdf

Policy Description: The Mississippi Drug Utilization Review Board proposed sending letters to providers treating patients receiving above 120 mg MEDD for 90 days or longer. Follow-up with a representative of the DUR to determine if this policy went into effect found that a similar policy did go into effect in September 2016, but letters are not sent to all providers prescribing above 120 mg MEDD. Rather, there is a limit to the number of letters sent each month.

Reason not included: Due to the limit of letters sent each month, the policy does not apply to all patients in the Medicaid population.

Reference: Big Data Analytics Cuts Medicaid Opioid Abuse, Ups Patient Safety. October 6, 2015. Health IT Analytics. https://healthitanalytics.com/news/big-data-analytics-cuts-medicaid-opioid-abuse-ups-patient-safety

Policy Description: Missouri has prior authorization requirements for quantity and days supply of certain opioid drugs. They also have begun to track some high dose prescribing.

Reason not included: There is no policy that includes an overall MEDD threshold across drugs.

Reference: North Dakota Department of Human Services Narcotics Authorization Algorithm. North Dakota Department of Human Services. http://www.hidesigns.com/assets/files/ndmedicaid/Criteria/2015/Visio-Narcotics.pdf

Policy Description: North Dakota requires prior authorization for certain drugs above dose of 150 MEDD, 200 MEDD, and 300 MEDD depending on the drug.

Reason not included: Only a small number of opioid drugs have the MEDD requirement and there is no total MEDD threshold.

Reference: Relates to prior authorization for opioids and Medicaid. Ohio HB 250. GA 131. (2015).

Policy Description: Proposed Bill in Ohio to implement Medicaid Prior Authorization requirement for all opioid prescriptions >80 MEDD.

Reason not included: The bill was introduced, but ultimately not passed.

Reference: Pennsylvania Guidelines on the Use of Opioids to Treat Chronic Noncancer Pain. Pennsylvania Medical Society. 2014.

Policy Description: Guidelines recommending against opioid prescribing above 100 MEDD without a specialist referral.

Reason not included: The Pennsylvania Medical Society would not be considered to be any of the types of organizations included in the study's inclusion criteria.

Appendix 2. Study protocol

I. Date of Protocol: November 11, 2017

II. Scope: A comprehensive survey of state-level Morphine Equivalent Daily Dose (MEDD) threshold policies. A doctoral candidate at Johns Hopkins researched and built this dataset under a dissertation grant from the Agency for Healthcare Research and Quality (AHRQ). To be included, the policy must meet all of the below inclusion criteria. The policy formats and state agencies selected were determined through an iterative process in which state level MEDD policies were searched for online and in the academic literature, and the list of included formats and agencies were updated to include the most common and frequently cited types of policies.

III. Primary Data Collection

- **a. Project Dates:** June 1, 2017-October 17, 2017. The doctoral candidate conducted preliminary background research for this project May 1, 2015 to May 31, 2016.
- **b. Dates Covered in the Dataset:** January 1, 2007- June 1, 2017. The published dataset only includes the most recent version of each state's policies, thus the published project is a cross-sectional dataset of state-level MEDD threshold policies in effect on June 1, 2017.
- **c. Data Collection Methods:** The research team consisted of the doctoral candidate (Researcher 1) who conducted preliminary background research, compiled the policy set, and coded the policies, a second researcher from the doctoral candidate's institution who independently coded the policies (Researcher 2), and Researcher 1's academic advisor who supervised the project (Supervisor).
- d. **Databases Used:** Researcher 1 used LexisNexis and Westlaw Next to conduct a comprehensive search of legislative acts in all 50 states and the District of Columbia. Researcher 1 used Google to find non-legislative state-level policy

documentation and checked each state's Medicaid Agency, Health Department, Prescription Drug Monitoring Program, Workers' Compensation Board/Division, Medical Board, and Pharmacy Board websites to determine if any other MEDD threshold policies existed.

e. Search Terms: "Morphine equivalent," "Milligrams morphine", "Opioid dose threshold," and "Opioid dose maximum."

f. Initial Returns and Additional Inclusion or Exclusion Criteria:

i. Policies must be of one of the following formats: "Guideline/Recommendation," "Legislative Act," "Rule/Regulation," "Prior Authorization," "Claim Denial," "Alert System/Automatic Patient Report" and have been implemented by one of the following state-level organizations: "Medicaid Agency," "Health Department," "Prescription Drug Monitoring Program," "State Legislature," "Workers' Compensation Board/Division," "Medical Board," or "Pharmacy Board." Policy formats and state-level organizations are defined later in this document.

ii. Policies from any private company or non-profit organization or from any type of national organization were not included unless they were co-sponsored by one of the above state-level organizations.

iii. Policies that reference policies implemented by other organizations (for example, in the background section of a report), but do not endorse the policy were not included.

iv. Policies that only limit the MEDD for certain drugs (e.g., non-preferred drugs only or short-acting drugs only) or do not limit cumulative MEDD were not included.

v. Medicaid and Workers' Compensation prior authorization policies that do not apply to all Medicaid or Workers' Compensation insurers within the state were not included.

vi. Policies which recommend increased follow-up after exceeding a given MEDD with no other recommended course of action were not included.

vii. Policies involving MEDD that did not meet inclusion criteria were compiled in a separate appendix, not published here, but should not be considered comprehensive.

IV. Coding

a. **Development of Coding Scheme:** Researcher 1 began with a number of a priori policy questions developed during the preliminary background research stage. As Researcher 1 compiled policy documentation and coded the policies, additional questions were added or modified with input from Researcher 2 and the Supervisor.

i. Dataset terminology:

- "Morphine Equivalent Daily Dose Policies" (hereafter "policy" or "policies") are policies which seek to limit overall opioid prescribing above a certain Morphine Equivalent Daily Dose (MEDD).

- "MEDD" is a measurement that converts opioid prescriptions to their equivalent dose in morphine and divides the total prescription by days supply (the number of days the prescription is intended to last). Policies may also refer to MEDD as Milligrams Morphine Equivalent (MME).

b. Coding Rules:

i. Policies were coded for each state and each state may have multiple policies. Where states have multiple policies, they are presented beginning with the most recent policy.

ii. The text coded was limited to MEDD Policies as previously defined. Other policies that were cited or cross-referenced in the policies were not coded or included in the policy source text.

iii. Below are explanations of individual coding questions and their respective responses.

- For the field "effective date"
  - For guidelines, when the guideline was first published. For all other policy formats, when the policy first became effective. For policies where only month and year are given, the first of the month is used, by default. When a state has multiple policies, the most recent is used for the effective date. For individual policy dates, refer to the questions "On what date did the policy become effective?"
- For the questions "What is the type of policy?"
  - "Guideline/recommendation" provides a recommended threshold over which prescribers should not exceed or should only exceed if special precautions are taken. Guidelines/recommendations have no mechanism of enforcement.
  - "Rules/regulations" are similar to guidelines, but are stated as an imperative (e.g., "must" "shall") and may or may not have an explicit means of enforcement.
  - "Legislative Act" is any law passed by the state's legislative body which has gone into effect. Proposed bills that never became law are not included.
  - "Prior Authorization" is a requirement that mandates prior approval from a third party before prescriptions above a given MEDD threshold may be filled. Legislation which establishes a prior authorization requirement was coded as "Prior Authorization" and caution noted.
  - "Alert System/Automatic Patient Report" is a mechanism by which targeted, unsolicited letters or alerts sent either by mail or electronically and inform prescribers that patients under their care have exceeded a given MEDD threshold. Follow-up action may or may not be required.

    - "Claim Denial" is a mechanism by which a third party denies prescription fills above a given MEDD threshold. In cases where Prior Authorization documentation explicitly states that prescriptions above a given MEDD threshold will not be approved, Prior Authorization and Claim Denial may be coded as two distinct policies.
- For the questions "Which organization(s) contributed to the policy?"
    - "Medicaid Agency" is a state-run organization primarily funded by the federal government which provides healthcare to qualifying low-income individuals.
    - "Health Department" is a state government agency which supports public health in the state. They are also often referred to as Departments of "Health and Social Services" or "Public Health."
    - "Prescription Drug Monitoring Program" (PDMP) collect prescribing and/or dispensing data of controlled substances including opioids. They may also be referred to as "Prescription Monitoring Programs."
    - "State Legislature" refers to a state's lawmaking body.
    - "Workers' Compensation Board/Division" is a state agency responsible for setting workers' compensation rules and regulations for the states. In some states, they may also provide workers' compensation insurance either exclusively or alongside private insurers.
    - "Medical Board" is a state government organization which is responsible for licensing medical professionals in the state.
    - "Pharmacy Board" is a state government organization which is responsible for licensing pharmacists in the state.
    - "Other" refers to any other organization that co-sponsored the policy. The names of these organizations are caution noted.
- For the questions "What is the MEDD threshold level?"
    - "MEDD threshold level" refers to the number of cumulative milligrams of morphine equivalent each day that the policy uses in the ways described above. If a range of values was given, the highest value in the range was used and the range was caution noted.
    - Policies that have a baseline MEDD threshold for all opioids, and then lower (stricter) MEDD thresholds for certain types of opioids were coded according to the baseline threshold. Where different threshold levels were associated with different patient group exemptions or different circumstances under which a threshold may be exceeded, each threshold level was considered a separate policy.

    - If two different thresholds were mentioned with no explicit differences in exemptions or circumstances under which the threshold should be exceeded, the lower of the two thresholds was selected.
- For the questions "Which types of patients, if any, are exempt from the policy?"
    - "Types of patients" refers to any patient population for whom the policy does not apply. For prior authorization, this specifically refers to individuals who do not need to go through the prior authorization process, regardless of whether these individuals will ultimately receive approval for the prescription.
    - "Acute/etiologic pain patients" was coded if the policy states that it does not apply to acute pain, that it does not apply to pain with a clear etiology or cause, or that it applies only to chronic pain.
    - "Terminal/hospice/palliative care patients" was coded if the policy states that it does not apply to any of the following: pain from a terminal condition, or individuals receiving hospice, palliative, or end-of-life care.
    - "Cancer/malignant pain patients" was coded if the policy states that it does not apply to patients with either cancer pain or malignant pain.
    - "Long-term care facility/nursing home patients" are exempt if the policy states that it does not apply to patients residing in either long-term care facilities or nursing homes.
    - "Patients with recent opioid use" are exempt if the policy states that it specifically applies to opioid naïve patients or new opioid prescriptions.
- For the questions "Are short courses of opioids excluded from the policy?"
    - "Short course" refers to opioid prescriptions that are below a given days supply and are intended for short-term use.
    - This question was coded "Yes" where the threshold policy did not apply to short courses of opioids.
- For the questions "How are short courses defined in number of days supply?"
    - Days supply is the maximum number of days the prescription(s) are intended to last.
    - Where the course was defined in the policy in months, this was coded in number of days with 30 days to a month assumed (e.g., 3 months = 90 days).
- For the questions "Under which circumstances may the MEDD threshold be exceeded?"

- Unless caution noted, it was assumed that the MEDD threshold may be exceeded if *any* of the indicated circumstances apply. Where multiple circumstances must apply in order for the threshold to be exceeded (e.g., Patient must receive drug testing *and* have pain contract/patient education) this was caution noted.
- "Specialist" refers to any specified (e.g., pain specialist, orthopedic specialist) or unspecified specialized physician. "Specialist consulted" means that a specialist must be consulted either prior to writing prescription(s) exceeding the MEDD threshold or that filling prescription(s) in excess of the MEDD threshold should trigger a specialist referral. Specialist referrals were coded when they were recommended or mandatory and documentation was or was not required.
- "Physician qualifications" was coded where there were any recommended or required qualifications that a physician should receive in order to write prescriptions in excess of the MEDD threshold.
- "Evidence of tapering" was coded where prescriptions in excess of the MEDD threshold may be written if the patient is receiving consecutively lower MEDD over time or the physician has put in place a plan to gradually lower the patients MEDD. This may be recommended or mandatory and documentation may or may not be required.
- "Patient has improved pain or function" was coded where prescriptions in excess of the MEDD threshold may be exceeded provided that the patient is experiencing decreased pain or increased function at the higher doses. This may be recommended or mandatory and documentation may or may not be required.
- "Clinical judgment" means that the MEDD threshold may be exceeded if the prescriber believes that there is a medical justification to do so. Documentation may or may not be required.
- "Prescription Drug Monitoring Programs" (PDMP) collect prescribing and/or dispensing data of controlled substances including opioids. Physicians or other authorized users may use these programs to view a patient's prescribing history and possibly detect doctor shopping. "PDMP is checked" means that the state's PDMP should be checked either prior to writing prescription(s) exceeding the MEDD threshold or that filling prescription(s) in excess of the MEDD threshold should trigger checking the PDMP. Checking the PDMP may be recommended or mandatory and documentation may or may not be required.
- "Pain contract/patient education" may refer to the required or recommended action of developing a contract with a patient

regarding proper use of opioids, educating patients on the risks of opioid use, working with patients to set realistic expectations about pain relief and practice self-management techniques, or any other risk mitigation strategy or change in treatment plan. This may occur prior to or after prescribing above the MEDD threshold, may be recommended or mandatory, and documentation may or may not be required.

- "Stable pain and function with non-escalating doses" means that the patient may exceed the MEDD threshold if they are not experiencing worse pain and function and if their MEDD has not increased. This criterion may be recommended or mandatory and documentation may or may not be required.
- "Legitimacy of prescription verified" applies specifically to policies for pharmacists. In this case, the pharmacist should verify the prescription with the patient's physician prior to dispensing the prescription if the MEDD exceeds a given threshold. This criterion may be recommended or mandatory and documentation may or may not be required.
- "Drug testing" may refer to the required or recommended action of testing a patient for narcotics use. This may occur prior to or after prescribing above the MEDD threshold, may be recommended or mandatory, and documentation may or may not be required.

V. Quality Control:

a. **Background Research**

The comprehensiveness of the list was verified in several ways:

- The list was checked against existing compilations of policies including the AHRQ guideline clearinghouse, The Brandeis Prescription Drug Monitoring Program (PDMP) Center of Excellence's 2016 report on PDMPs with unsolicited reporting, the National Alliance for Model State Drug Laws 2016 report on State Pain Management and Prescribing Policies, and the University of Wisconsin Pain and Policy Studies Group's 2015 Report on Profiles of State Policies Governing Drug Control and Medical Pharmacy Practice.
- Medicaid policies were checked against Medicaid Drug Utilization Review Annual Report Surveys, which lists states with Medicaid agencies responding "yes" to the question, "Have you set recommended maximum morphine equivalent daily dose measures?"
- The list was checked against academic literature using the above search terms, for references to MEDD threshold policies.
- For states with no MEDD threshold policy found, at least one representative from a relevant state health agency was contacted to confirm the lack of a formal policy.

b. **Coding**

Policy questions were reviewed by the Supervisor and questions were edited for clarity. Researcher 2 suggested additional modifications to questions during a preliminary coding of the first three state's policies. Modifications were agreed upon by the two coders. Researchers 1 and 2 then redundantly coded 100% of the policies. Agreement rates were calculated and disagreements were arbitrated by the Supervisor. Research 1 and 2 independently coded the first eight policies (alphabetically by state) and had a divergence rate of 33%. Divergent codes were discussed and resolved and clarifying edits were then made to the codebook based on divergent answers. The two researchers then independently coded the remaining policies and had a divergence rate of 21% and repeated the process of resolving differences in coding and clarifying the codebook based on divergent answers. Divergence rates were calculated October 23, 2017. When answers to questions were ambiguous in a policy as noted by one or both coders, an attempt was made to clarify the coded element with a representative of the relevant state organization.

Appendix 3. Codebook

1. Does the state have at least one type of MEDD policy? (**MEDDPolicy1, binary**)
   1.1. What is the type of policy? (**Type1, categorical, mutually exclusive**; options: *"Guideline," "Legislative Act," "Rule/Regulation," "Prior Authorization," "Claim Denial," "Alert System/Automatic Patient Report")*
   1.2. On what date did the policy become effective? (**Date1, date)**
   1.3. Which organization(s) contributed to the policy? (**Organization1, categorical, check all that apply**; options: *"Medicaid Agency," "Health Department," "Prescription Drug Monitoring Program," "State Legislature," "Workers' Compensation Board/Division," "Medical Board," "Pharmacy Board," "Other"*)
   1.4. What is the MEDD threshold level? (**Threshold1, numerical**)
   1.5. Which types of patients, if any, are exempt from the policy? (**PatientsExempt1, categorical, check all that apply**; options: *"Cancer/malignant pain patients," "Sickle cell anemia patients," "Acute/etiologic pain patients," "Inpatient care patients," "Terminal/hospice/palliative care patients," "HIV/AIDS patients," "Long-term care facility/nursing home patients," "Emergency room care patients," "Intra-operative care patients," "Patients with recent opioid use," "None apply"*)
   1.6. Are short courses of opioids excluded from the policy? (**ShortCourse1, binary**)
      1.6.1. How are short courses defined in number of days supply? (**DaysSupply1, numerical**)
   1.7. Under which circumstances, if any, may the MEDD threshold be exceeded? (**CircumstancesExceeded1, categorical, check all that apply**; options: *"Specialist consulted," "Physician qualifications," "Evidence of tapering," "Patient has improved pain or function," "Clinical judgment," "Prescription Drug Monitoring Program is checked," "Pain contract/patient education," "Stable pain and function with non-escalating doses," "Legitimacy of prescription verified," "Drug testing," "None apply"*)
2. Does the state have at least two types of MEDD policy? (**binary**)
   2.1. What is the type of policy? (**categorical, mutually exclusive** options: *"Guideline," "Legislative Act," "Rule/Regulation," "Prior Authorization," "Claim Denial," "Alert System/Automatic Patient Report"*)
   2.2. On what date did the policy become effective? (**date)**
   2.3. Which organization(s) contributed to the policy? (**categorical, check all that apply** options: *"Medicaid Agency," "Health Department," "Prescription Drug Monitoring Program," "State Legislature," "Workers' Compensation Board/Division," "Medical Board," "Pharmacy Board," "Other"*)
   2.4. What is the MEDD threshold level? (**numerical**)
   2.5. Which types of patients, if any, are exempt from the policy? **(categorical, check all that apply**; options: *"Cancer/malignant pain patients," "Sickle cell anemia patients," "Acute/etiologic pain patients," "Inpatient care patients," "Terminal/hospice/palliative care patients," "HIV/AIDS patients," "Long-term care facility/nursing home patients," "Emergency room care patients," "Intra-operative care patients," "Patients with recent opioid use," "None apply"*)
   2.6. Are short courses of opioids excluded from the policy? (**binary**)
      2.6.1. How are short courses defined in number of days supply? (**numerical**)

2.7. Under which circumstances, if any, may the MEDD threshold be exceeded? (**categorical, check all that apply**; options: *"Specialist consulted," "Physician qualifications," "Evidence of tapering," "Patient has improved pain or function," "Clinical judgment," "Prescription Drug Monitoring Program is checked," "Pain contract/patient education," "Stable pain and function with non-escalating doses," "Legitimacy of prescription verified," None apply"*)

3. Does the state have at least three types of MEDD policy? (**binary**)
   3.1. What is the type of policy? (**categorical, mutually exclusive;** options: *"Guideline," "Legislative Act," "Rule/Regulation," "Prior Authorization," "Claim Denial," "Alert System/Automatic Patient Report"*)
   3.2. On what date did the policy become effective? (**date)**
   3.3. Which organization(s) contributed to the policy? (**categorical, check all that apply;** options: *"Medicaid Agency," "Health Department," "Prescription Drug Monitoring Program," "State Legislature," "Workers' Compensation Board/Division," "Medical Board," "Pharmacy Board," "Other"*)
   3.4. What is the MEDD threshold level? (**numerical**)
   3.5. Which types of patients, if any, are exempt from the policy? (**categorical, check all that apply**; options: *"Cancer/malignant pain patients," "Sickle cell anemia patients," "Acute/etiologic pain patients," "Inpatient care patients," "Terminal/hospice/palliative care patients," "HIV/AIDS patients," "Long-term care facility/nursing home patients," "Emergency room care patients," "Intra-operative care patients," "Patients with recent opioid use," "None apply"*)
   3.6. Are short courses of opioids excluded from the policy? (**binary**)
      3.6.1. How are short courses defined in number of days supply? (**numerical**)
   3.7. Under which circumstances, if any, may the MEDD threshold be exceeded? (**categorical, check all that apply**; options: *"Specialist consulted," "Physician qualifications," "Evidence of tapering," "Patient has improved pain or function," "Clinical judgment," "Prescription Drug Monitoring Program is checked," "Pain contract/patient education," "Stable pain and function with non-escalating doses," "Legitimacy of prescription verified," "None apply"*)

Chapter 3. The Impact of Morphine Equivalent Daily Dose Threshold Guidelines on Prescribed Dose in a Workers' Compensation Population

Introduction

Prescription opioids are used to effectively treat pain following injury, but carry a high risk of addiction and may result in overdose and death when taken at high doses or combined with other drugs. Prescription opioid-related mortality has doubled in the United States between 2002 and 2016.[65] Non-medical opioid use and addiction are of particular concern among those receiving prescriptions through workers' compensation insurance. Workers often initiate opioid use following occupational injury and complications of opioid use, such as the development of an opioid use disorder, may delay return to work, increase utilization of other medical resources, and result in other adverse outcomes for employees.[30,31] Previous research has found opioid use to be very common among injured workers. In a study of US workers' compensation claims 2000-2010, around one-third of workers with a time-loss shoulder or back injury receiving opioids, and nearly half of those patients went on to become long-term opioid users (>3 months of continuous use).[32] Furthermore, research suggests that opioid users receiving workers' compensation insurance, across all injuries, are more likely to receive high doses and to become chronic users than are opioid users in the general population.[33]

Previous research has also established that high-dose opioid prescribing is a major risk factor for opioid overdose.[66–68] Given this association, a commonly promoted tool to address the prescription opioid overdose epidemic is the establishment of Morphine Equivalent Daily Dose (MEDD) threshold guidelines. A number of state-level agencies, insurers, and organizations have promoted these types of policies. Among these organizations are state workers' compensation

organizations including Washington, Massachusetts, Connecticut, New York, and California, which have all passed MEDD threshold guidelines. MEDD, is a measurement that converts opioid prescriptions to their equivalent dose in morphine and divides the total prescription by days supply (the number of days the prescription is intended to last),[43] allowing comparison among different types of opioid formulations and strengths. MEDD threshold guidelines set an overall dose over which prescribing is not recommended.

Despite the proliferation of these guidelines, evaluations of the impact of MEDD guidelines on prescribing practices have been limited to Washington State. Evaluations of Washington's MEDD threshold guideline in the Medicaid population found a reduction in opioid use from pre- to post- guideline implementation with the greatest reductions occurring in the proportion of patients receiving over 120 MEDD, which was the threshold level set by the Washington guideline.[57,71] The studies did not make use of comparison states, but did note that the reduction was seen at a time in which opioid prescribing was increasing in the United States, overall. However, in another study using Washington workers' compensation claims data, no statistically significant reduction in opioid poisonings and adverse events was observed following the passage of MEDD threshold guidelines, although these events may have been under-reported.[81] The goal of the present study is to evaluate the impact of two states' MEDD threshold guidelines (Massachusetts and Connecticut) on the MEDD of filled prescriptions paid for by workers' compensation insurance.

Methods

To evaluate the impact of workers' compensation MEDD threshold guidelines, administrative claims data, 2000-2013, from a large, national workers' compensation insurer was used. These data have been used previously to evaluate occupational injury clinical practice guidelines.[32,82–84] The data includes National Drug Codes (NDC), drug quantities, dates of service, International Classification of Disease, Version 9 (ICD9) codes, state, age, sex, and employment status prior to injury.

Study Population

To be included in the study, patients must be age 16-64, have a lost-time injury after January 1, 2000, and have had at least one valid, active opioid prescription between January 1, 2010 and December 31, 2013. Valid opioid prescriptions were defined as having non-missing units and days supply. Units with values of 0 or >1000 and days supply 0 or >180 were considered missing, consistent with prior studies.[85] Duplicate values (based on NDC, units, and fill date) were deleted. Opioid prescriptions and morphine equivalent conversion factors were identified using a crosswalk file from the Centers for Disease Control. Patients must reside in a treatment state (Massachusetts and Connecticut) or control state (Illinois, Indiana, and Pennsylvania). Control states were selected on the basis of not implementing Prescription Drug Monitoring Programs (PDMPs) or passing any major prescription opioid legislation during the study period and having parallel monthly MEDD trends prior to guideline implementation. Treatment states were selected if they enacted a workers' compensation MEDD policy, as defined in Chapter 2, during the study period. States with monopolistic workers' compensation, meaning that the state runs their own workers' compensation program for most workers, were not included as control or treatment states due to limited and non-representative presence in the data, which consisted of

claims data from a private insurer. Individuals with missing covariate data (<5%) were also excluded.

Outcomes

The primary outcome for this study was MEDD calculated at the person-month level by multiplying quantity, dose, and conversion factor and dividing by days supply, taking into account multiple and overlapping prescriptions. SAS code and an example of the MEDD calculation are provided in the Appendix. As the distribution of MEDD is highly skewed right, the natural log of MEDD was also tested as an outcome. MEDD dichotomized as >120 or ≤120 and >90 or ≤90 were also tested, corresponding to the guideline thresholds for Massachusetts and Connecticut, respectively.

Policy Variables

Policy variables were defined in two ways: First, as a simple pre- and post- indicator for whether or not the policy was in effect during the given month. Second, a months since policy implementation variable was developed to allow for gradual policy dissemination over time. Massachusetts' guideline was implemented February 2012 and Connecticut's was implemented July 2012.

Individual Level Variables

In addition to age, sex, and full-time employment status, a number of derived variables were included in the analysis. These include high baseline opioid use (defined as >90 MEDD and >120 MEDD in at least one month prior to February 2012, which was the first policy implementation date), time since first opioid prescription (to account for within-subject changes

in MEDD), six body region Abbreviated Injury Scores (AIS) which were calculated from ICD9 codes using ICDPIC for Stata14.[6] Injury Severity Score (ISS), a summary measure that squares and adds the three highest AIS score, also calculated using ICDPIC, was also calculated for descriptive purposes. Because ICDPIC does not include ICD9 codes for burns, a separate burn indicator was created defined as ICD9 codes with the first three digits 940-949.[86] Indicators for whether or not the patient received an acute pain diagnosis and whether or not the patient had a cancer diagnosis, as defined by Mack et al.[85], were also created.

Analyses

Generalized linear mixed models were used with MEDD as the primary outcome and person-month as the unit of analysis. All models included state fixed effects, a linear time trend, and clustering at the individual and state level which account for correlated outcomes within individuals and within states. All models included controls for age, sex, six body region AIS, burn indicator, and months since the first opioid prescription. Policy variables tested included both dichotomous and months in effect variables as described in the previous section. All time variables (months since first opioid prescription, months since policy implementation, and the monthly linear time trend) were tested for multicollinearity, defined as variance inflation factors (VIF) >10. Models were stratified by months with no active opioid prescription in the previous month (new prescription months) and months with an opioid prescription in the previous month (continuing prescription months) to determine if the policy had a differential effect in these two groups. Models were stratified by the presence of acute pain diagnosis and by the presence of a cancer diagnosis. The Massachusetts policy is specifically geared towards chronic pain and, while neither the Massachusetts nor the Connecticut policy explicitly excludes cancer patients, MEDD policies typically are geared towards non-cancer pain.(Chapter 2) It was hypothesized

that these policies would have either or no effect or a smaller effect in acute pain and cancer patients than in those with chronic, non-cancer pain. Models were also stratified by high baseline opioid use with larger effects of the policy hypothesized in individuals with high baseline use.

Results

Population characteristics by treatment group (control states, treatment states pre-policy implementation, and treatment states post-policy implementation) are presented in Table 1. The majority of individuals across all groups were male and had at least one acute pain diagnosis. Significant differences existed between treatment groups with a higher percentage of males in the treatment states (83.0% post-policy and 76.5% pre-policy) as compared to the control states (74.3%) ($p<0.001$). Individuals in the control states were more likely to be employed full-time prior to injury (92.6% in control states, 88.9% in treatment states pre-policy, and 89.7% in treatment states post-policy, $p<0.001$) and have an acute pain diagnosis (95.2% in control states, 94.0% in treatment states pre-policy, and 93.1% in treatment states post-policy, $p<0.001$). Individuals in treatment states were on average older (43.9 (SD 10.7) in control states, 44.1 (SD 10.7) in treatment states pre-policy implementation and 47.0 (SD 9.2) in treatment states post-policy implementation, $p<0.001$) and had higher Injury Severity Scores (ISS) (3.7 (SD 4.5) in control states, 4.1 (SD 5.5) in treatment states pre-policy and 4.6 (SD 5.9) in treatment states post-policy, $p<0.001$). A greater proportion of person-months involved high-dose opioid use in treatment states than in control states and the percentage of individuals with high-dose opioid use increased from the pre- to the post-period (15.9% with MEDD >120 in control states, 17.3% in treatment states pre-policy and 23.6% in treatment states post-policy, $p<0.001$) (Table 2). There was also a higher percentage of new opioid prescription months in control states than in

treatment states (10.2% in control states, 8.6% in treatment states pre-policy and 3.6% in treatment states post-policy, $p<0.001$).

Unadjusted MEDD by state and month are presented in Figure 1. Prior to the first MEDD guideline implementation in Massachusetts, the control and treatment states had roughly parallel trends in monthly MEDD use. Average MEDD increased relatively linearly each month with a higher baseline MEDD in Massachusetts than in Connecticut or the control states. Following the passage of the Massachusetts guideline, average MEDD continued to increase for a couple of months before leveling off and finally decreasing. In Connecticut, average MEDD use appears to increase at a slower rate than in the control states following the passage of the Connecticut guideline and begins to level off and decrease slightly in 2013.

Regression results for the entire population using both dichotomous and months in effect policy definitions are presented in Table 3. After adjusting for covariates, policy implementation was associated with a 9.26 mg decrease in MEDD (95% CI: -13.96, -4.56) from the pre- to post-period, relative to control states. Decrease in MEDD also became more pronounced over time. Policy implementation was associated with a 1.87 mg decrease in MEDD for each month since the policy's implementation (95% CI: -2.37, 1.37, $p<0.001$).

Using the natural log of MEDD and dichotomous MEDD outcome variables did not change the direction or significance of the relationship (Appendix, Tables 1-3). Using a dichotomous policy definition and log MEDD, policy implementation was associated with an 11% decrease in MEDD relative to control states (Appendix, Table1). Stratified analyses are presented in full in

Appendix Tables 4-13 and summarized in Figure 2. As hypothesized, the policy was associated with larger decreases in MEDD among individuals without an acute pain diagnosis as compared to with an acute pain diagnosis, among individuals without a cancer diagnosis as compared to with a cancer diagnosis, and among patients with high baseline opioid use as compared to patients with no high baseline opioid use. Continuing opioid prescriptions saw larger increases than did new opioid prescriptions. When examining state guidelines individually, both the guidelines in Massachusetts and Connecticut were associated with significant decreases in MEDD relative to control states. However, the magnitude of these decreases were larger in Massachusetts than in Connecticut.

Discussion

Overall, the passage of MEDD threshold guidelines was associated with a decrease in the MEDD of filled prescriptions relative to control states. The magnitude of this reduction was greater the more months the policy was in effect. Additionally, there was a larger decrease in MEDD among the groups that the policy was intended to target, namely patients with chronic, non-cancer pain and high baseline use. Importantly, no statistically significant change in MEDD was observed among cancer patients—alleviating a common concern that these types of policies may prevent individuals with cancer from receiving adequate pain treatment. While significant reductions were observed in both states that passed guidelines, larger decreases were observed in Massachusetts than in Connecticut. It is unclear why larger decreases were observed in Massachusetts. Notably, Massachusetts had a higher MEDD threshold than Connecticut. It is possible that dissemination efforts in Massachusetts were more robust and identifying differences in dissemination and influence, perhaps using surveys or qualitative methods, is an

important topic for future research. Understanding the relationship between threshold level and impact on prescriber behavior is also an important topic for future research. It is possible that setting the threshold level too high may prevent at-risk patients from being identified, while setting the threshold too low may discourage providers from complying.

This study has a number of important strengths, namely a large sample size and a study design that utilizes pre- and post- data from both treatment and control states. The dataset also contained diagnosis codes which allowed controls for injury severity and stratification by clinically important groups.

Notable limitations include a dynamic policy environment in which a number of efforts to curb opioid prescribing are present. While the study carefully selected control states that had not passed major opioid legislation, implemented PDMPs, or implemented other types of MEDD policies during the study period, there are still a number of other important considerations. Efforts to restrict opioid prescribing at the local level were not systematically captured and, if present, may have influenced results. It was also assumed that national-level policy efforts did not differentially influence prescribing by state, but this assumption may not be valid. As with most claims data research from a single insurer, it is important to note that opioids not paid for by the workers' compensation insurer are not captured. Additionally, the results of this study may not be generalizable to the workers' compensation population as a whole and future work should seek to replicate evaluations of MEDD threshold guidelines in other populations.

High dose prescribing is an important risk factor for opioid-related mortality, but it is not the only one. A number of recent policies are increasingly emphasizing the importance of limiting days supply of new opioid prescriptions to prevent addiction and long-term use as well as the use of alternative non-opioid pain treatment and management.[52] There is also some concern that restriction of opioid use among long-term opioid users may lead to increased use of heroin or other illicit drugs, though evidence on this is mixed.[87–89] Future research should examine the impact of these guidelines on patient outcomes to determine if reduction of MEDD leads to reductions in overdose and addiction, or if other factors offset the reduction of a single risk factor.

Tables

Table 1. Population characteristics by treatment group, N=6,562 people (66,656 person-months)

	Control states, N=4,482 people (40,149 person-months)	**Treatment states**, **pre-policy**[a], N=2,034 people (19,457 person-months)	**Treatment states, post-policy**[a], N=698 people (7,050 person-months)	**p-value**[b]
State, N (%)				
MA	N/A	1412 (69.4%)	517 (74.1%)	N/A
CT	N/A	622 (30.6%)	181 (25.9%)	N/A
IL	1990 (44.4%)	N/A	N/A	N/A
IN	549 (12.3%)	N/A	N/A	N/A
PA	1,943 (43.7%)	N/A	N/A	N/A
Male, N (%)	3,329 (74.3%)	1,555 (76.5%)	579 (83.0%)	<0.001
Full-time	4,148 (92.6%)	1,809 (88.9%)	626 (89.7%)	<0.001
Age, Mean (SD)	43.9 (10.7)	44.1 (10.7)	47.0 (9.2)	<0.001
Acute pain diagnosis, N (%)	4,265 (95.2%)	1,912 (94.0%)	650 (93.1%)	0.03
ISS, Mean (SD)	3.7 (4.5)	4.1 (5.5)	4.6 (5.9)	<0.001

[a]Individuals in treatment states may be counted in pre-policy period, post-policy period, or both
[b]Chi-square test for categorical variables and one-way ANOVA for continuous variables
Abbreviation: ISS, Injury Severity Score

Table 2. AIG person-month characteristics by treatment group, N=66,656 person-months (6,562 people)

	Control states, N=40,149 person-months (4,482 people)	Treatment states, pre-policy implementation[a] N=19,457 person-months (2,034 people)	Treatment states, post policy implementation[a], N=7,050 person-months (698 people)	p-value[b]
Months >120 MEDD, N (%)	6,374 (15.9%)	3,371 (17.3%)	1,665 (23.6%)	<0.001
Months >90 MEDD, N (%)	7,860 (19.6%)	4,264 (21.9%)	2,040 (28.9%)	<0.001
% New rx months	4,102 (10.2%)	1,663 (8.6%)	252 (3.6%)	<0.001

a. Individuals in treatment states may be counted in pre-policy period, post-policy period, or both
b. Chi-square test

Table 3. Regression results, continuous MEDD outcome with dichotomous and months policy in effect definitions, all patients (N=66,656 person-months)

	Dichotomous policy definition			Months in effect policy definition		
Variable	**Estimate**	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
Policy variable	-9.26	(-13.96, -4.56)	<.001	-1.87	(-2.37, -1.37)	<.001
Head AIS	0.80	(-0.83, 2.42)	0.337	0.81	(-0.82, 2.44)	0.329
Face AIS	2.68	(-1.80, 7.17)	0.241	2.58	(-1.90, 7.07)	0.259
Chest AIS	-3.49	(-5.53, -1.46)	<.001	-3.53	(-5.57, -1.49)	<.001
Abdomen AIS	10.80	(9.03, 12.56)	<.001	10.77	(9.00, 12.53)	<.001
Extremities AIS	0.51	(-0.65, 1.67)	0.386	0.49	(-0.67, 1.65)	0.411
External AIS	13.69	(11.28, 16.10)	<.001	13.58	(11.17, 15.99)	<.001
Burn indicator	-30.66	(-44.29, -17.04	<.001	-30.52	(-44.13, -16.90	<.001
Age	-0.98	(-1.10, -0.87)	<.001	-0.98	(-1.10, -0.86)	<.001
Male	17.56	(14.80, 20.32)	<.001	17.58	(14.82, 20.34)	<.001
Months after Jan 2012	0.65	(0.54, 0.77)	<.001	0.73	(0.62, 0.85)	<.001
Full-time employee	21.30	(17.21, 25.40)	<.001	21.30	(17.20, 25.40)	<.001
CT (reference=PA)	-13.00	(-17.04, -8.97)	<.001	-12.95	(-16.92, -8.98)	<.001
IL (reference=PA)	-20.27	(-23.27, -17.27	<.001	-20.26	(-23.25, -17.26	<.001
IN (reference=PA)	-23.32	(-29.33, -17.31	<.001	-23.06	(-29.07, -17.05	<.001
MA (reference=PA)	6.16	(2.81, 9.51)	<.001	7.55	(4.28, 10.81)	<.001
Months since first opioid rx	0.73	(0.68, 0.78)	<.001	0.73	(0.68, 0.78)	<.001

Abbreviations: AIS, Abbreviated Injury Score

Figures

Figure 1. Mean MEDD by policy with loess smoothing (smooth=0.2)

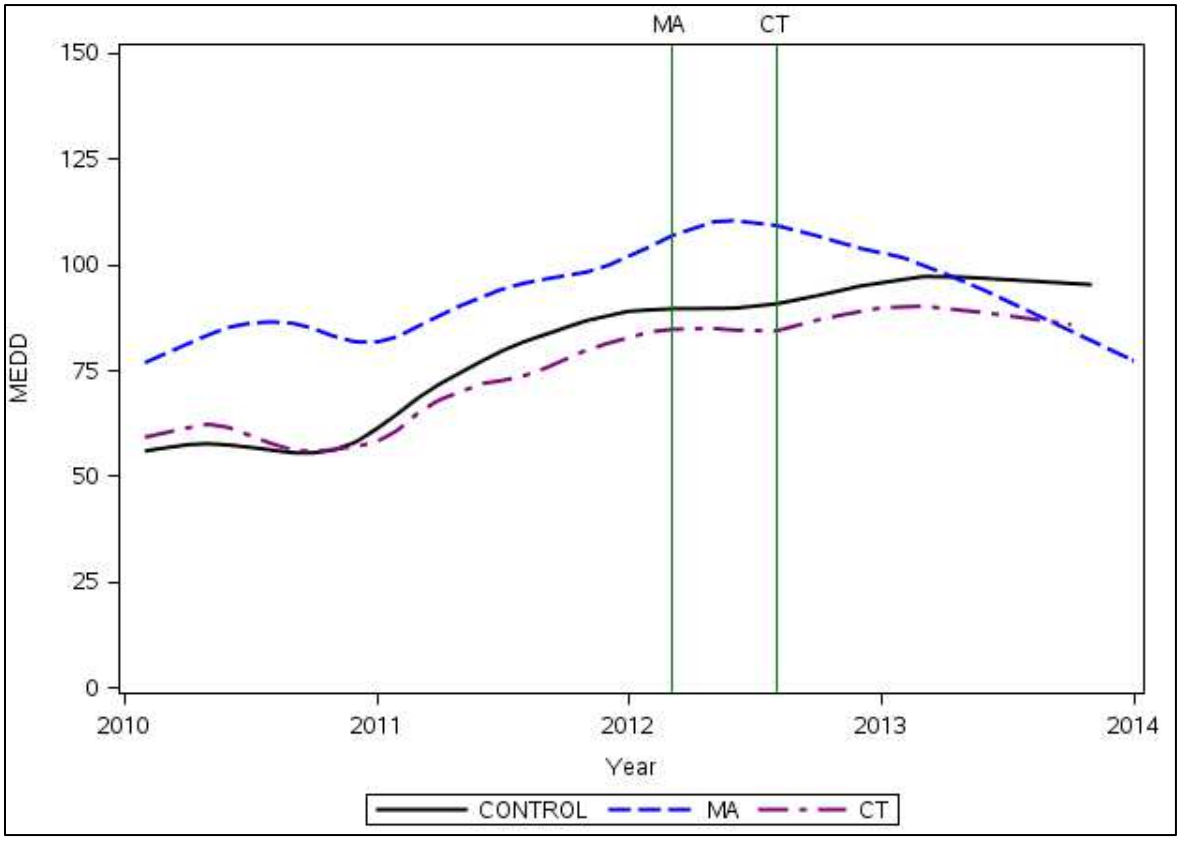
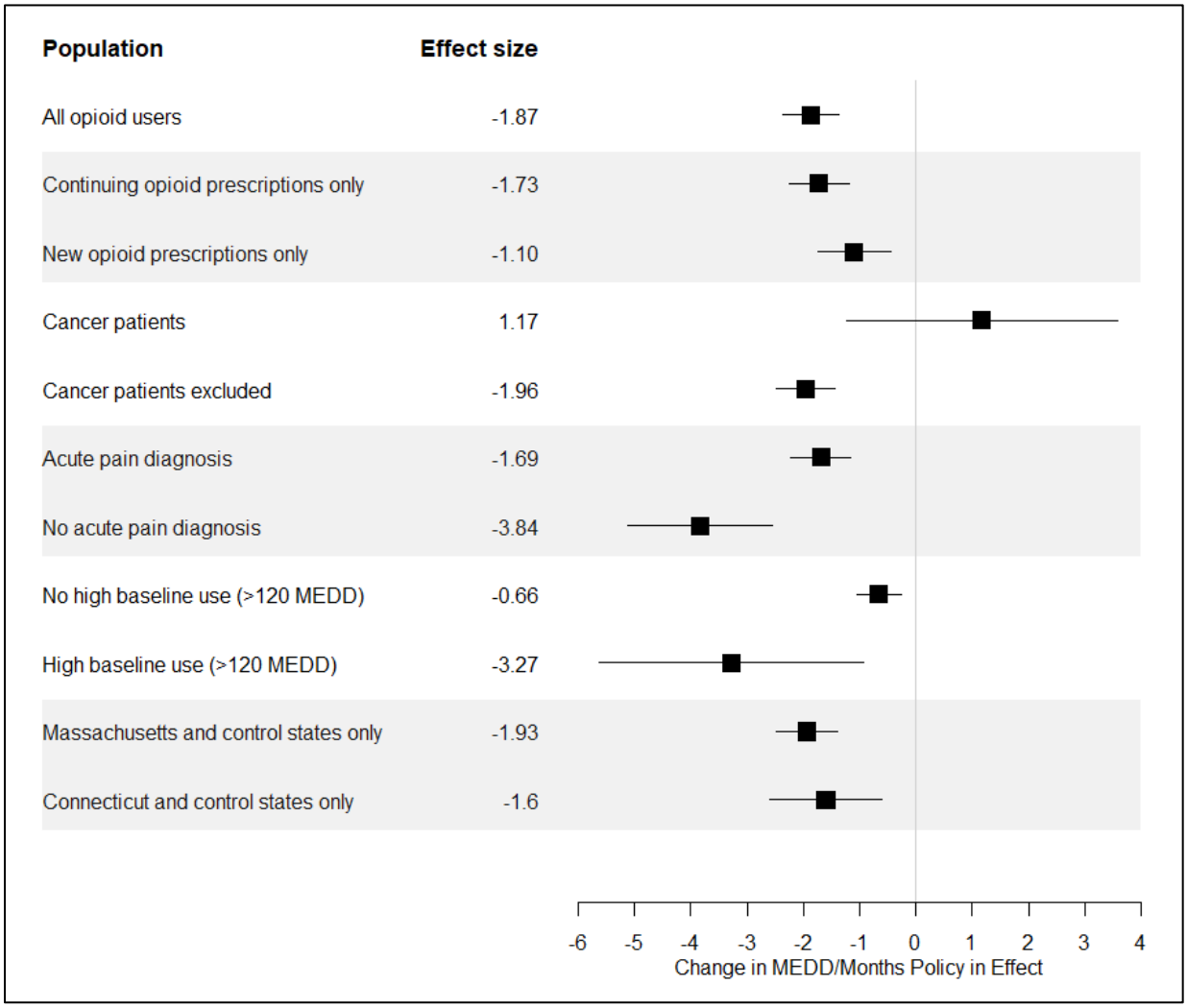


Figure 2. Summary of stratified analyses



Appendix

Appendix 1. SAS Code for sample MEDD calculation

Variable definitions
Enrolid: Unique patient identifier
Svcdate: Date prescription filled
Daysupp: Days supply of prescription
Strength: Mg per one unit count
Metqty: Number of units of drug
Mmecon: Conversion factor to milligrams morphine equivalent

```
data opioidrx;
input enrolid $ svcdate daysupp strength metqty mmecon;
datalines;
100 10JAN2010 15 15 30 1
100 20JAN2010 90 180 10 1
100 21JAN2010 10 10 15 1.5
100 05FEB2010 60 30 50 1
100 06MAR2010 1 5 10 7
;

data calendar;
  length key 8;
  do dt = "01JAN2010"d to "31DEC2015"d;
  month=month(dt);
  year=year(dt);
   key + 1;
    output;
  end;
  format dt date9.;
run;

data opioidrx;
set opioidrx;
end_dt=svcdate+daysupp;
MEDD_rx=(strength*mmecon*metqty)/daysupp;
run;

proc sql;
create table monthly_opioid_analysis as
SELECT enrolid, month, year
, COUNT(distinct cats(enrolid, dt)) as days_ttl, sum(MEDD_rx) as MEDD_ttl
  FROM calendar c
  JOIN opioidrx x
    ON c.dt > x.svcdate
   AND c.dt <= end_dt
 GROUP BY enrolid, year, month;
 quit;

 data monthly_opioid_analysis;
 set monthly_opioid_analysis;
 MEDD=MEDD_ttl/days_ttl;
 run;
```

Appendix 2. Example of MEDD calculation for a patient

Rx Number	Prescription fill date	Days supply	Quantity	Strength	Conversion Factor
1	01/10/2010	15	15	30	1
2	01/20/2010	90	180	10	1
3	01/21/2010	10	10	15	1.5
4	02/05/2010	60	30	50	1
5	03/06/2010	1	5	10	7

- In January, the patient has 22 active days of opioid prescription (15 days from Rx1, 12 days from Rx2, 11 days from Rx3 with overlapping days). The patient has 15 days at 30 mg morphine equivalent/day ((15 pills*30 mg/pill*1 mg morphine equivalents/mg)/15 days) from Rx1, 12 days at 20 mg morphine equivalents/day ((180 pills*10 mg/pill*1 mg morphine equivalents/mg)/90 days) from Rx2, 11 days at 20.45 mg morphine equivalents/day ((10 pills*15 mg/pill*1.5 mg morphine equivalents/mg)/11 days). **This results in a MEDD of 41.59 for the month of January** ((15 days*30 mg morphine equivalents/day)+(12 days*20 mg morphine equivalents/day)+(11 days*20.45 mg morphine equivalents/day)/22 active days.
- In February, the patient has 28 active days of opioid prescription (28 days from Rx2 and 24 days from Rx4 with overlapping days). The patient has 28 days at 20 mg morphine equivalents a day ((180 pills*10 mg*1 mg morphine equivalent/mg)/90 days) from Rx2 and 24 days at 25 mg morphine equivalents a day ((30 pills*50 mg*1 mg morphine equivalent/mg)/60 days) from Rx4. **This results in a MEDD of 41.43 for the month of February** ((28 days*20 mg morphine equivalents/day)+(24 days*25 mg morphine equivalents/day))/28 active days.
- In March, the patient has 31 active days of opioid prescription (31 days from Rx2, 31 days from Rx4, and 1 day from Rx5 with overlapping days). The patient has 20 days at 20 mg morphine equivalents a day ((180 pills*10 mg*1 mg morphine equivalents/mg)/90 days) from Rx2, 31 days at 25 mg morphine equivalents a day ((30 pills*50 mg*1 mg morphine equivalent/mg)/60 days) from Rx4, and 1 day at 350 mg morphine equivalents a day ((5 pills*10 mg* 7 mg morphine equivalents a day)/1 day). **This results in a MEDD of 56.29 for the month of March** ((31 days*20 mg morphine equivalent/day)+(31 days*25 mg morphine equivalent/day))+(1 day*350 mg morphine equivalent/day))/31 active days.
- In April, the patient has 19 active days of opioid prescription (19 days from Rx2 and 15 days from Rx4 with overlapping days). The patient has 19 days at 20 MEDD (180 pills*10 mg*1 mg morphine equilavent/mg)/90 days from Rx2 and 15 days at 25 mg morphine equivalents a day ((30 pills*50 mg*1 mg morphine equivalent/mg)/60 days) from Rx4. **This results in a MEDD of 26.58 for the month of April.**

Table 1. Regression results, Log MEDD outcome, dichotomous policy variable, all patients (N=66,656 person-months)

Variable	Estimate	95% CI	p-value
Policy	-0.12	(-0.15, -0.09)	<.001
Head AIS	0.04	(0.03, 0.05)	<.001
Face AIS	0.04	(0.01, 0.07)	0.011
Chest AIS	-0.06	(-0.07, -0.04)	<.001
Abdomen AIS	0.16	(0.14, 0.17)	<.001
Extremities AIS	-0.00	(-0.01, 0.00)	0.317
External AIS	0.12	(0.10, 0.13)	<.001
Burn indicator	-0.19	(-0.28, -0.09)	<.001
Age	-0.01	(-0.01, -0.00)	<.001
Male	0.19	(0.17, 0.21)	<.001
Months after Jan 2012	0.01	(0.01, 0.01)	<.001
Full-time employee	0.19	(0.16, 0.22)	<.001
CT (reference=PA)	-0.09	(-0.12, -0.07)	<.001
IL (reference=PA)	-0.10	(-0.13, -0.08)	<.001
IN (reference=PA)	-0.12	(-0.17, -0.08)	<.001
MA (reference=PA)	0.11	(0.08, 0.13)	<.001
Months since first opioid rx	0.00	(0.00, 0.01)	<.001

Table 2. Regression results, MEDD >120 outcome, dichotomous policy variable, all patients (N=66,656 person-months)

Variable	Estimate	95% CI	p-value
Policy	-0.26	(-0.33, -0.18)	<.001
Head AIS	0.11	(0.09, 0.14)	<.001
Face AIS	0.24	(0.18, 0.31)	<.001
Chest AIS	-0.15	(-0.19, -0.12)	<.001
Abdomen AIS	0.31	(0.29, 0.34)	<.001
Extremities AIS	0.06	(0.03, 0.08)	<.001
External AIS	0.14	(0.10, 0.19)	<.001
Burn indicator	-0.57	(-0.88, -0.26)	<.001
Age	-0.02	(-0.02, -0.01)	<.001
Male	0.46	(0.40, 0.52)	<.001
Months after Jan 2012	0.02	(0.02, 0.02)	<.001
Full-time employee	0.39	(0.30, 0.48)	<.001
CT (reference=PA)	-0.09	(-0.16, -0.02)	0.008
IL (reference=PA)	-0.44	(-0.49, -0.38)	<.001
IN (reference=PA)	-0.48	(-0.62, -0.34)	<.001
MA (reference=PA)	0.05	(-0.00, 0.11)	0.059
Months since first opioid rx	0.01	(0.01, 0.01)	<.001

Table 3. Regression results, MEDD >90 outcome, dichotomous policy variable, all patients (N=66,656 person-months)

Variable	Estimate	95% CI	p-value
Policy	-0.27	(-0.34, -0.20)	<.001
Head AIS	0.12	(0.09, 0.14)	<.001
Face AIS	0.17	(0.10, 0.23)	<.001
Chest AIS	-0.16	(-0.19, -0.13)	<.001
Abdomen AIS	0.30	(0.28, 0.33)	<.001
Extremities AIS	0.04	(0.02, 0.06)	<.001
External AIS	0.17	(0.13, 0.21)	<.001
Burn indicator	-0.21	(-0.44, 0.02)	0.069
Age	-0.02	(-0.02, -0.01)	<.001
Male	0.38	(0.33, 0.44)	<.001
Months after Jan 2012	0.02	(0.02, 0.02)	<.001
Full-time employee	0.43	(0.35, 0.52)	<.001
CT (reference=PA)	-0.05	(-0.12, 0.01)	0.111
IL (reference=PA)	-0.43	(-0.49, -0.38)	<.001
IN (reference=PA)	-0.45	(-0.58, -0.32)	<.001
MA (reference=PA)	0.11	(0.06, 0.16)	<.001
Months since first opioid rx	0.01	(0.01, 0.01)	<.001

Table 4. Regression results, continuous MEDD outcome, months policy in effect, continuing prescription months (N=60,639 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	-1.73	(-2.26, -1.19)	<.001
Head AIS	0.60	(-1.15, 2.36)	0.502
Face AIS	2.68	(-2.16, 7.53)	0.278
Chest AIS	-3.92	(-6.11, -1.72)	<.001
Abdomen AIS	10.12	(8.22, 12.02)	<.001
Extremities AIS	0.45	(-0.81, 1.72)	0.483
External AIS	13.20	(10.54, 15.85)	<.001
Burn indicator	-33.73	(-48.98, -18.49	<.001
Age	-1.19	(-1.32, -1.06)	<.001
Male	18.40	(15.36, 21.43)	<.001
Months after Jan 2012	0.60	(0.48, 0.73)	<.001
Full-time employee	22.79	(18.31, 27.27)	<.001
CT (reference=PA)	-14.78	(-19.11, -10.45	<.001
IL (reference=PA)	-23.06	(-26.34, -19.77	<.001
IN (reference=PA)	-24.22	(-31.11, -17.33	<.001
MA (reference=PA)	6.22	(2.65, 9.79)	<.001
Months since first opioid rx	0.71	(0.66, 0.77)	<.001

Table 5. Regression results, continuous MEDD outcome, months policy in effect, new prescription months (N=6,017 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	-1.10	(-1.75, -0.45)	<.001
Head AIS	1.03	(-0.47, 2.52)	0.180
Face AIS	-0.31	(-4.38, 3.77)	0.883
Chest AIS	1.15	(-0.81, 3.12)	0.249
Abdomen AIS	3.93	(2.18, 5.68)	<.001
Extremities AIS	0.81	(-0.17, 1.80)	0.105
External AIS	2.36	(0.52, 4.19)	0.012
Burn indicator	3.89	(-5.20, 12.98)	0.402
Age	0.05	(-0.04, 0.13)	0.273
Male	2.71	(0.64, 4.79)	0.010
Months after Jan 2012	0.50	(0.39, 0.61)	<.001
Full-time employee	4.36	(1.09, 7.63)	0.009
CT (reference=PA)	-0.47	(-3.74, 2.79)	0.776
IL (reference=PA)	0.71	(-1.62, 3.04)	0.551
IN (reference=PA)	-0.69	(-4.25, 2.88)	0.705
MA (reference=PA)	6.77	(4.14, 9.40)	<.001
Months since first opioid rx	0.02	(-0.04, 0.08)	0.556

Table 6. Regression results, continuous MEDD outcome, months policy in effect, patients with cancer diagnosis (N=2,484 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	1.17	(-1.24, 3.58)	0.340
Head AIS	16.49	(8.67, 24.30)	<.001
Face AIS	26.23	(8.20, 44.27)	0.004
Chest AIS	-31.24	(-38.68, -23.79	<.001
Abdomen AIS	16.10	(9.35, 22.85)	<.001
Extremities AIS	-11.47	(-16.71, -6.23)	<.001
External AIS	18.17	(5.90, 30.43)	0.004
Burn indicator	22.08	(-14.68, 58.84)	0.239
Age	0.54	(-0.03, 1.11)	0.062
Male	84.54	(70.20, 98.89)	<.001
Months after Jan 2012	-0.39	(-0.92, 0.13)	0.144
Full-time employee	53.23	(33.66, 72.80)	<.001
CT (reference=PA)	22.57	(4.21, 40.92)	0.016
IL (reference=PA)	-61.44	(-75.55, -47.34	<.001
IN (reference=PA)	-4.48	(-33.92, 24.96)	0.766
MA (reference=PA)	6.31	(-8.48, 21.09)	0.403
Months since first opioid rx	0.36	(0.17, 0.54)	<.001

Table 7. Regression results, continuous MEDD outcome, months policy in effect, patients with no cancer diagnosis (N=64,172 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	-1.96	(-2.47, -1.45)	<.001
Head AIS	-0.32	(-1.99, 1.34)	0.704
Face AIS	-0.54	(-5.20, 4.11)	0.819
Chest AIS	-2.54	(-4.68, -0.41)	0.019
Abdomen AIS	10.46	(8.63, 12.30)	<.001
Extremities AIS	0.60	(-0.59, 1.80)	0.322
External AIS	13.87	(11.41, 16.33)	<.001
Burn indicator	-38.12	(-52.99, -23.25	<.001
Age	-1.04	(-1.16, -0.92)	<.001
Male	15.71	(12.90, 18.52)	<.001
Months after Jan 2012	0.78	(0.67, 0.90)	<.001
Full-time employee	20.14	(15.95, 24.33)	<.001
CT (reference=PA)	-13.94	(-18.01, -9.87)	<.001
IL (reference=PA)	-18.53	(-21.59, -15.46	<.001
IN (reference=PA)	-22.79	(-28.91, -16.66	<.001
MA (reference=PA)	8.07	(4.73, 11.41)	<.001
Months since first opioid rx	0.74	(0.68, 0.79)	<.001

Table 8. Regression results, continuous MEDD outcome, months policy in effect, patients with acute pain diagnosis (N=63,394 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	-1.69	(-2.22, -1.17)	<.001
Head AIS	1.08	(-0.57, 2.73)	0.199
Face AIS	2.84	(-1.70, 7.38)	0.220
Chest AIS	-3.67	(-5.73, -1.61)	<.001
Abdomen AIS	11.28	(9.47, 13.09)	<.001
Extremities AIS	1.24	(0.02, 2.46)	0.046
External AIS	15.68	(13.11, 18.26)	<.001
Burn indicator	-30.61	(-44.40, -16.83	<.001
Age	-1.02	(-1.14, -0.89)	<.001
Male	19.57	(16.71, 22.42)	<.001
Months after Jan 2012	0.68	(0.56, 0.80)	<.001
Full-time employee	20.17	(15.93, 24.40)	<.001
CT (reference=PA)	-11.11	(-15.20, -7.02)	<.001
IL (reference=PA)	-19.77	(-22.86, -16.67	<.001
IN (reference=PA)	-21.84	(-28.03, -15.65	<.001
MA (reference=PA)	9.23	(5.85, 12.61)	<.001
Months since first opioid rx	0.77	(0.72, 0.83)	<.001

Table 9. Regression results, continuous MEDD outcome, months policy in effect, patients with no acute pain diagnosis (N=3,262 person-months)

Variable	Estimate	995% CI	p-value
Months Policy in Effect	-3.84	(-5.12, -2.56)	<.001
Age	-0.69	(-1.08, -0.29)	<.001
Male	-24.74	(-33.70, -15.78	<.001
Months after Jan 2012	1.65	(1.28, 2.02)	<.001
Full-time employee	40.22	(26.57, 53.88)	<.001
CT (reference=PA)	-85.44	(-100.44, -70.4	<.001
IL (reference=PA)	-55.68	(-66.46, -44.91	<.001
IN (reference=PA)	-87.70	(-109.86, -65.5	<.001
MA (reference=PA)	-42.40	(-53.36, -31.43	<.001
Months since first opioid rx	0.03	(-0.10, 0.17)	0.635

Table 10. Regression results, continuous MEDD outcome, months policy in effect, patients with no high baseline use (>120 MEDD) (N=9,629 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	-0.66	(-1.05, -0.26)	0.001
Head AIS	0.12	(-1.12, 1.36)	0.850
Face AIS	-7.41	(-11.04, -3.79)	<.001
Chest AIS	-2.49	(-4.09, -0.90)	0.002
Abdomen AIS	3.84	(2.36, 5.32)	<.001
Extremities AIS	-1.82	(-2.74, -0.90)	<.001
External AIS	-7.86	(-9.80, -5.92)	<.001
Burn indicator	-3.14	(-21.73, 15.45)	0.741
Age	-0.17	(-0.27, -0.08)	<.001
Male	7.44	(5.21, 9.67)	<.001
Months after Jan 2012	1.29	(1.04, 1.54)	<.001
Full-time employee	5.18	(1.99, 8.37)	0.001
CT (reference=PA)	-14.57	(-17.95, -11.18	<.001
IL (reference=PA)	-13.22	(-15.64, -10.80	<.001
IN (reference=PA)	-1.36	(-7.45, 4.74)	0.663
MA (reference=PA)	-4.93	(-8.90, -0.96)	0.015
Months since first opioid rx	-0.17	(-0.21, -0.13)	<.001

Table 11. Regression results, continuous MEDD outcome, months policy in effect, patients with high baseline use (>120 MEDD) (N=5,767 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	-3.27	(-5.62, -0.93)	0.006
Head AIS	-13.56	(-20.53, -6.58)	<.001
Face AIS	8.99	(-11.58, 29.56)	0.392
Chest AIS	4.81	(-4.74, 14.36)	0.323
Abdomen AIS	-18.28	(-25.75, -10.81	<.001
Extremities AIS	0.24	(-5.25, 5.74)	0.931
External AIS	24.17	(11.59, 36.75)	<.001
Burn indicator	-152.65	(-214.59, -90.7	<.001
Age	-2.75	(-3.38, -2.13)	<.001
Male	19.88	(5.05, 34.71)	0.009
Months after Jan 2012	-2.07	(-3.63, -0.51)	0.009
Full-time employee	64.58	(40.92, 88.25)	<.001
CT (reference=PA)	-49.84	(-70.65, -29.04	<.001
IL (reference=PA)	-79.12	(-94.55, -63.69	<.001
IN (reference=PA)	-97.40	(-133.02, -61.7	<.001
MA (reference=PA)	-6.59	(-30.86, 17.69)	0.595
Months since first opioid rx	1.27	(1.07, 1.47)	<.001

Table 12. Regression results, continuous MEDD outcome, months policy in effect, Massachusetts and control states (N=58,966 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	-1.93	(-2.47, -1.39)	<.001
Head AIS	2.10	(0.32, 3.87)	0.020
Face AIS	-5.11	(-10.06, -0.17)	0.043
Chest AIS	-3.61	(-5.85, -1.37)	0.002
Abdomen AIS	11.69	(9.73, 13.65)	<.001
Extremities AIS	-0.45	(-1.70, 0.81)	0.486
External AIS	14.40	(11.76, 17.03)	<.001
Burn indicator	-32.09	(-46.32, -17.86	<.001
Age	-1.13	(-1.26, -1.00)	<.001
Male	17.85	(14.80, 20.89)	<.001
Months after Jan 2012	0.73	(0.60, 0.85)	<.001
Full-time employee	18.84	(14.37, 23.31)	<.001
IL (reference=PA)	-20.06	(-23.14, -16.97	<.001
IN (reference=PA)	-22.77	(-28.95, -16.59	<.001
MA (reference=PA)	7.60	(4.21, 10.98)	<.001
Months since first opioid rx	0.76	(0.70, 0.82)	<.001

Table 13. Regression results, continuous MEDD outcome, months policy in effect, Connecticut and control states (N=47,839 person-months)

Variable	Estimate	95% CI	p-value
Months Policy in Effect	-1.60	(-2.60, -0.60)	0.002
Head AIS	2.39	(0.82, 3.96)	0.003
Face AIS	6.24	(2.02, 10.47)	0.004
Chest AIS	-7.78	(-9.71, -5.86)	<.001
Abdomen AIS	16.42	(14.77, 18.07)	<.001
Extremities AIS	2.46	(1.38, 3.54)	<.001
External AIS	-0.69	(-2.94, 1.57)	0.551
Burn indicator	-12.28	(-24.45, -0.12)	0.048
Age	-0.37	(-0.48, -0.26)	<.001
Male	10.47	(8.01, 12.93)	<.001
Months after Jan 2012	0.84	(0.74, 0.93)	<.001
Full-time employee	14.34	(10.22, 18.45)	<.001
CT (reference=PA)	-14.90	(-18.15, -11.64	<.001
IL (reference=PA)	-19.96	(-22.32, -17.61	<.001
IN (reference=PA)	-23.85	(-28.56, -19.14	<.001
Months since first opioid rx	0.59	(0.54, 0.63)	<.001

Chapter 4. The Impact of Morphine Equivalent Daily Dose Threshold Policies on Prescribed Dose in a Privately Insured Population

Introduction

Prescription opioids are an effective means of treating pain, but are frequently misused and may result in overdose and death when taken at high doses or combined with other drugs. Prescription opioid-related mortality has doubled in the United States between 2002 and 2016[65] and previous research has established that high-dose opioid prescribing is a major risk factor for opioid overdose.[66–68] Given this association, a commonly promoted tool to address the prescription opioid overdose epidemic is the establishment of Morphine Equivalent Daily Dose (MEDD) threshold policies. MEDD, is a measurement that converts opioid prescriptions to their equivalent dose in morphine and divides the total prescription by days supply, the number of days the prescription is intended to last,[43] allowing comparison among different opioid formulations and strengths. MEDD threshold policies set an overall dose over which prescribing is discouraged in some way, though the threshold level and type of policy varies widely by the states and organizations that promote them. These types of policies are typically not implemented in isolation, but rather as part of a comprehensive strategy on opioid prescription reform. From January 1, 2007 to June 1, 2016, 31 MEDD policies have been enacted by 22 states (Chapter 2).

Despite the proliferation of MEDD policies, evaluations of their impact have been limited. Evaluations of Washington's MEDD threshold guideline in the Medicaid population found a reduction in opioid use from pre- to post- guideline implementation with the greatest reductions occurring in the proportion of patients receiving over 120 MEDD, (the threshold level set by the

guideline).[57,71] The studies did not make use of comparison states, but did note that the reduction was seen at a time in which opioid prescribing was increasing in the United States, overall. Chapter 3 examined the impact of prescribed MEDD dose following the passage of workers' compensation MEDD threshold guidelines in Connecticut and Massachusetts and found an 11% reduction in mg MEDD of filled opioid prescriptions following guideline passage relative to control states. To date, no studies of MEDD threshold policies have been conducted in the private insurance population and it is unknown whether policies targeted at the general population will have the same effects as those targeted at specific populations, such as Medicaid or Workers' Compensation claimants, where payers may have more of an influence on prescribing practices. Furthermore, the impact of MEDD policies other than guidelines on prescribed dose have not been studied, though research in other contexts suggests that they may be more impactful than guidelines. For example, studies have generally found that adherence to published prescribing guidelines is low, even years after a guideline has been published,[58–61] but, passive alert systems—systems that provide notifications to prescribers through EHR decision support, e-mail, or mailed letters—tended to significantly improve provider adherence to prescribing guidelines.[58–60,62,63] The goal of the present study is to evaluate the impact of nine states' MEDD threshold policies on the MEDD of filled prescriptions among individuals with private insurance. These policies include guidelines, rules/regulations/legislative acts, and passive alert systems.

Methods

Data

Truven MarketScan© data was used to evaluate state-level policies implemented between January 1, 2010 and December 31, 2015. This dataset consists of commercial claims, both inpatient and outpatient, from 350 private payers. The data contains International Classification of Disease, Version 9 (ICD9) codes, discharge codes, facility codes, National Drug Codes (NDC), quantity of drug, days supply of drug, age, sex, and state of enrollee residence. MarketScan® commercial claims data has been previously used to conduct research on opioid utilization[90] and the data are weighted by Truven Health to be representative of individuals in the United States with employer-sponsored health insurance.[91]

Population

To determine whether passage of policies was associated with change in the odds of receiving any opioids, analyses were conducted on a random sample of one million enrollees under the age of 65 from a treatment or control state (Figure 1). Individuals 65 and older were excluded, as these individuals may also have Medicare claims for opioid prescriptions, which are not observable in the data.

Additional analyses were conducted on the entire population of enrollees under the age of 65 from a treatment or control state with at least one valid, active opioid prescription between January 1, 2010 and December 31, 2015. Control states were selected on the basis of not implementing Prescription Drug Monitoring Programs (PDMPs) or passing any major prescription opioid legislation during the study period and parallel trends in MEDD prior to implementation of the first policy (January 2012).

Outcomes

All outcomes were related to receipt or MEDD of valid, filled opioid prescriptions. Both receipt of any opioids and dose of opioids among those who received opioids were tested as outcomes to distinguish between potential effects of the MEDD threshold levels specifically and other co-occurring policy features.

Valid opioid prescriptions were defined as having non-missing quantities and days supply. Quantities with values of 0 or >1000 and days supply 0 or >180 were considered missing, consistent with prior studies.[85] Due to discrepancies in the reporting of drug quantities, some quantities were misreported by a factor of ten and a cleaning protocol was implemented wherein certain values were modified. For example, the common quantity of 30 pills was often misreported as 300. This cleaning protocol is described in detail in Appendix 1. Duplicate values (based on NDC, units, and fill date) were deleted. Opioid prescriptions and morphine equivalent conversion factors were identified using a crosswalk file from the Centers for Disease Control.[92] Among the sample of one million enrollees, three outcomes were tested: Indicators for whether or not an enrollee had any opioid use, opioid use >60 MEDD, and opioid use >120 MEDD during a month in which the individual was enrolled. MEDD was calculated at the person-month level by multiplying quantity, dose, and conversion factor and dividing by days supply, taking into account multiple and overlapping prescriptions. SAS code and an example of the MEDD calculation is provided in Appendix 1-2 of Chapter 2.

Among the population of enrollees with any opioid use, the primary outcome of interest was average monthly MEDD. As the distribution of MEDD is highly skewed right, log transformed

MEDD was also tested as an outcome. MEDD dichotomized at the 120, 100, 80, and 60 MEDD threshold levels were also tested, corresponding to the thresholds used by the policies of the nine treatment states in this study (Table 1).

Policies

The policies examined in this study have been described in detail in Chapter 2. Briefly, policy types include guidelines, rules/regulations, legislative acts, and passive alert systems, with guidelines theorized to be less impactful than other types of policies. The policy types, threshold levels, and populations specifically excluded from the policy are detailed in Table 1. Policy variables were defined in two ways: First, as a simple pre- and post- indicator for whether or not the policy was in effect at the time. Second, a months since policy implementation variable was developed to allow for gradual policy dissemination over time. The timeline for policy implementation is shown in Figure 1. Policy variables were also defined as "any policy" and stratified by whether the policy was a "guideline" or a "strong policy" based on their theorized impact. Strong policies included rules/regulations, legislative acts, and passive alert systems. With the exception of two states, states only implemented one type of policy. Arizona implemented a strong policy prior to implementing a guideline. In analyses, the strong policy takes precedence over the guideline, so Arizona was not included stratified analyses including only guidelines. Washington implemented a guideline prior to the study period (2007) and implemented a strong policy during the study period (2012). Similar to Arizona, Washington was not included in the stratified analyses containing only guidelines.

Individual Level Variables

In addition to age and sex, a number of derived variables were included in the analysis. These include high baseline opioid use—defined as four indicator variables corresponding to the four MEDD thresholds used: 60 MEDD, 80 MEDD, 100 MEDD, and 120 MEDD—in at least one month prior to January 2012, which was the first policy implementation date. Time since first opioid prescription was also created to account for within-subject changes in MEDD. A number of indicators were created to account for patient populations that are explicitly excluded from some policies. These excluded patient groups, which were systematically identified in Chapter 2, include patients with cancer, acute pain, terminal/hospice/palliative patients, inpatients, and short courses of opioids. Patients were defined as acute pain or cancer if they had at least one relevant ICD9 code on either an inpatient or outpatient claim during the study period as defined by Mack et al.[85] Patients with any inpatient claims during the study period were defined as inpatients, patients with any hospice facility codes, revenue codes, or a hospice discharge status during the study period were defined as terminal/hospice/palliative care. Patients with any emergency room or long-term care facility revenue or facility codes during the study period were defined as emergency room and long-term care facility patients, respectively. Any months in which there were no opioid prescriptions in the prior two months were considered short courses opioids, consistent with the policy definitions of short courses as less than three months.

Analyses

An interrupted time series with comparison states approach was used to evaluate the relationship between policy implementation and opioid use. First, generalized linear mixed models with a logit link were used with the dichotomous outcomes of any opioid use, MEDD>60 and MEDD>120 in the random sample of one million enrollees using dichotomous guideline and strong policy indicators interacted with time. The unit of analysis was person-month and controls

for age and sex, state fixed effects, a linear time trend, and clustering and the individual and state level, which accounts for correlated outcomes within states and individuals, were included.

Among enrollees with any opioid use, generalized linear mixed models were used with MEDD as the primary outcome and person-month as the unit of analysis. All models included state fixed effects and clustering at the individual and state level, which account for outcomes within individuals and within states being correlated. Models included controls for age, sex, and months since the first opioid prescription. A linear time trend with a spline at January, 2014 was included based on plots of MEDD outcomes over time (Appendix Figures 1-4). Policy variables tested included both dichotomous and months in effect variables as described in the previous section. All time variables including months since first opioid prescription, months since policy implementation, and the monthly linear time trend were tested for multicollinearity, defined as variance inflation factors (VIF) >10. Models were stratified by all previously defined exclusion groups with the hypothesis that larger decreases in MEDD would be observed in the groups not excluded from the policies while excluded groups would see little to no change, relative to the control group. Models were also stratified by high baseline dose defined as at least month with a MEDD above each of the four designated thresholds prior to 2012. It was hypothesized that larger decreases in MEDD would be seen among individuals with high baseline use as compared to those without high baseline use. Individual regression analyses were also run for each state using both continuous and dichotomous MEDD outcomes according to each state's policy threshold and stratified by each state's specific patient group exclusions.

Sensitivity Analyses

Great care was taken to examine the opioid policy environment in the states and years selected for inclusion into the analysis. The greatest historical threat to validity identified was in Washington, which launched a PDMP within a month of the passage of its MEDD threshold legislative act. Therefore, analyses were conducted with and without Washington. All other PDMPs in control and treatment states became active outside of the study period. Among opioid users, the MEDD outcome was tested as continuous, log transformed, and dichotomous (60, 80, 100, 120) and policy variables were also tested as dichotomous and months policy in effect to allow for the possibility of an implementation lag.

Results

Baseline—defined as months prior to January 2012—demographic, enrollment, and opioid use characteristics of a random sample of enrollees by policy state (control, guideline, or strong policy) are presented in Table 2. Of the one million individuals in the sample, 719,568 individuals were enrolled prior to 2012 and are included in the baseline table. Demographic and enrollment characteristics were similar among all three groups with females comprising slightly more than half of enrollees, average age ranging from 30.67 (strong policy states) to 32.62 (control states), and an average of 19.80 months (strong policy states) to 19.88 months of enrollment over two years. However, individuals in the strong policy states had higher opioid use at baseline with 19.29% of enrollees filling at least one opioid prescription prior to 2012 in strong policy states as compared to 15.89% in control states and 15.43% in guideline states. Similarly, enrollees in strong policy states were more likely to have filled at least one prescription >60 MEDD or >120 MEDD than enrollees in control or guideline states.

Among individuals with at least one opioid prescription during the study period, the final population for analysis was 27,391,637 person-months representing 7,030,785 individuals. Of these individuals, 4,961,599 had at least one opioid prescription filled prior to January 2012. Baseline characteristics of these users by policy state are presented in Table 3. In general, opioid users, regardless of policy state, were older and more likely to be female than the overall population of enrollees. As with the overall population of enrollees, baseline demographic characteristics of opioid users did not differ greatly by policy state. Opioid users in strong policy states were more likely than opioid users in control or guideline states to have high dose use defined as >60 MEDD (28.86% in strong policy states vs. 25.46% in control states and 25.28% in guideline states) and >120 MEDD (7.48% in strong policy states vs. 6.44% in guideline states and 6.45% in control states). In all policy states, a majority of opioid users had at least one exclusion—defined as an acute pain or cancer diagnosis, or hospice, inpatient, long-term care, or emergency department use during the study period, but opioid users in strong policy states were less likely to have one of these exclusions (56.96%) as compared to opioid users in guideline (58.62%) or control states (62.07%).

Among all enrollees, the unadjusted proportion of a sample of enrollees receiving any opioid, opioids >60 MEDD, and opioids >120 MEDD decreased across all three policy groups over time (Figure 2). A higher proportion of enrollees in strong policy states received any opioids and high dose opioids than did enrollees in guideline and control states, but the proportion of enrollees with any opioid use appears to have decreased more rapidly in the strong policy states than in the guideline or control states.

Regression results using the dichotomous outcomes of any opioid use, MEDD>60, and MEDD>120 on a random sample of one million enrollees are presented in Table 4. Across all three outcomes, the odds of any opioid use and high dose opioid use decreased over time with 0.6% lower odds of any opioid use, 0.9% lower odds of opioid use >60 MEDD and >120 MEDD each month. Passage of both guidelines and strong policies were associated with lower odds of any opioid use relative to control states. Guideline passage was associated with 15% lower odds of any opioid use (95% CI: 18% lower to 13% lower, $p<0.001$) and strong policy passage was associated with 15% lower odds of any opioid use (18% lower to 12% lower, $p<0.001$) relative to control states. However, neither guideline passage nor strong policy passage was associated with a change in odds of high dose use relative to control states.

Several additional regression analyses were conducted among opioid users in treatment and control states. These included analyses using continuous, log transformed, and dichotomous MEDD outcomes and policy variables that allowed for lagged dissemination, and excluding Washington State. Results of these regressions are presented in Tables 1-8 of the Appendix. Among opioid users policy passage was associated with a small but statistically significant increase in MEDD (3.72 mg MEDD, 95% CI: 3.51, 3.92; $p<0.001$) (Appendix, Table 1). The direction and significance of this relationship did not change after excluding Washington State or from using different outcome and policy definitions. Each month the policy was in effect was associated with a 0.08 mg MEDD increase relative to control states, (95% CI: 0.07, 0.09; $p<0.001$) (Appendix, Table 4).

A number of stratified regression analyses were also conducted including separate analyses by policy type (guideline or strong policy) and exclusion groups. The results of these analyses are presented in Tables 9-32 of the Appendix and summarized in Figure 3. In each of the stratified analyses, the direction and significance of the relationship between policy and MEDD was consistent, although the magnitude of the relationship was larger in some excluded groups (hospice, cancer diagnosis, inpatient, long-term care) and smaller in other excluded groups (short courses of opioids and patients with acute pain diagnoses). Among patients with any exclusion, the policy was associated with a 3.10 mg MEDD increase relative to control states (95% CI: 2.90, 3.31; $p<0.001$)(Appendix, Table 31) and among patients with no exclusions, the policy was associated with a 5.44 mg MEDD increase (95% CI: 4.92, 5.95; $p<0.001$).

Individual regressions where each state was individually compared to control states were also performed. Due to reporting restrictions in the MarketScan© data use agreement, the results from individual states may not be presented. Therefore, a summary of state-level results are presented in Table 5. In guideline states, guideline passage was associated with increased odds of any opioid use in one state and decreased odds of any opioid use in three states. Similarly, in strong policy states, policy passage was associated with increased odds of any opioid use in one state and decreased odds of any opioid use in four states. However, when looking specifically at change in dose among opioid users, guideline passage was associated with increased MEDD in all states, regardless of outcome or exclusions. In strong policy states, the associations between policy passage and MEDD among opioid users were mixed. Policy passage was associated with increased MEDD in one state, decreased MEDD in another state, and no significant relationship

with MEDD in the remaining three states. Results were also mixed when examining dichotomous outcomes and stratification by state-specific exclusion groups.

Discussion

Overall, both guidelines and strong policies were associated with lower odds of using opioids relative to control states. However, there was no statistically significant relationship between either type of policy and high dose opioid use. Among opioid users, there was actually a small, but statistically significant increase in dose, and excluding certain individuals for whom the policy was not specifically targeted did not change the magnitude or direction of the relationship. The small increase in dose may have been due to lower proportions of individuals receiving any opioids leaving only patients with higher pain management needs still receiving opioids. It is possible that MEDD thresholds as part of a larger set of opioid policies and accompanied by an increased awareness of the risks of opioid prescribing may have led to a decrease in the proportion of individuals prescribed opioids. However, there is no evidence that the policies successfully targeted high dose use or individuals with chronic, non-cancer pain. There was also no evidence that policies with a higher theorized impact—rules/regulations, legislative acts, and passive alert systems—had a greater impact on prescribed MEDD than did guidelines. Therefore, it is unlikely that any observed changes in overall opioid prescribing were due specifically to setting MEDD thresholds.

This study had a number of important strengths, including a large, multi-state study population. This allowed for adequate sample size, even in the smallest sample subgroups, for example, individuals receiving hospice care. The study also makes use of longitudinal data over a period

of six years and includes pre- and post- periods for multiple policies of interest. The analysis improves upon prior evaluations of MEDD policies by making use of comparison states. This study also builds upon previous work which systematically examined policy structure, threshold level, and excluded groups and used this information to evaluate several different aspects of the policies.

This study must also be evaluated in light of its limitations. From 2010 to 2016, the United States has experienced a complex and dynamic policy environment surrounding opioids. While care was taken to select states that did not pass major opioid legislation, MEDD policies, or implement PDMPs, policies at the local level were not systematically captured and may have had an influence in certain states. Individual insurers are also increasingly instituting a variety of coverage and utilization management policies to reduce high risk opioid use and some of these practices may include use of MEDD thresholds, which may bias the results. It is also important to note that only opioids from commercial claims covered by MarketScan© were observed. It was not possible to observe if individuals obtained opioids from other payers or sources.

This study is an important first step in understanding how state-level MEDD policies may influence opioid prescribing in privately insured populations. Future work should evaluate the impact of MEDD policies in other contexts and populations. In particular, Medicaid prior authorization requirements which utilize MEDD thresholds have not been evaluated. In addition to evaluating the impact of MEDD policies on prescribing behavior, further research should evaluate their impact on patient outcomes. Surveys or qualitative research may illustrate

differences in dissemination efforts and policy awareness and help understand why certain policies are more influential.

Tables

Table 1. Thresholds, policy types, and excluded patient groups in state policies

State	Threshold	Policy Type	Excluded patient groups
AZ (03/14)	120	Legislative act	Inpatients
IN	60	Rule/Regulation	Acute pain, terminal/hospice/palliative, long-term care facility, short courses
RI	120	Rule/Regulation	Acute pain
TN	120	Passive alert system	Acute pain, terminal/hospice/palliative, inpatient, emergency room
WA (01/12)	120	Legislative act	Acute pain
AZ (11/14)	100	Guideline	Acute pain and terminal/hospice/palliative patients, short courses
CA	80	Guideline	Acute pain, terminal/hospice/palliative
CO	120	Guideline	Cancer, terminal/hospice/palliative
OH	80	Guideline	Acute pain, terminal/hospice/palliative, short courses
SC	80	Guideline	None
WA (04/07)	120	Guideline	Acute pain, cancer

Table 2. Baseline characteristics of all users by policy type (Random sample of enrollees, months prior to January 2012, N=719,568 enrollees)

	Control States (N=193,416)	Guideline States (N=363,177)	Strong Policy States (N=162,975)
Male, N(%)	96,058 (49.66)	178,359 (49.11)	80,056 (49.12)
Age, Mean (SD)	32.62 (18.27)	31.36 (18.30)	30.67 (18.46)
Any opioid use, N(%)	30,740 (15.89)	56,044 (15.43)	31,432 (19.29)
≥1 month >60 MEDD	7,698 (3.98)	14,324 (3.94)	9,058 (5.56)
≥1 month >120 MEDD	1,978 (1.02)	3,703 (1.02)	2,328 (1.43)
Months enrolled, Mean (SD)	19.88 (12.07)	20.93 (12.39)	19.80 (12.18)

Table 3. Baseline characteristics of opioid users by policy type (Individuals using opioids prior to January 2012, N=4,961,599 enrollees)

	Control States (N=1,287,321)	Guideline States (N=2,356,122)	Strong Policy States (N=1,318,303)
Male, N(%)	575,690 (44.72)	1,034,102 (43.89)	575,835 (43.68)
Age, Mean (SD)	40.30 (15.52)	40.22 (15.44)	39.94 (15.80)
≥1 month >60 MEDD, N(%)	327,737 (25.46)	595,474 (25.28)	380,447 (28.86)
≥1 month >120 MEDD, N(%)	82,971 (6.45)	151,763 (6.44)	98,549 (7.48)
Months with ≥1 opioid, Mean (SD)	3.29 (5.48)	3.55 (5.95)	3.66 (5.96)
Acute pain diagnosis, N(%)	448,458 (34.84)	749,220 (31.80)	394,538 (29.93)
Cancer diagnosis, N(%)	206,204 (16.02)	355,930 (15.11)	187,757 (14.24)
Hospice, N(%)	4,058 (0.32)	5,712 (0.24)	3,883 (0.29)
Inpatient visit, N(%)	197,693 (15.36)	354,727 (15.06)	191,035 (14.49)
Long-term care, N(%)	5,852 (0.45)	8,255 (0.35)	3,777 (0.29)
ED visit, N(%)	388,058 (30.14)	616,931 (26.19)	350,476 (26.59)
Any person-level exclusion, N(%)	799,066 (62.07)	1,381,147 (58.62)	750,952 (56.96)

Abbreviations: ED, Emergency Department; MEDD, Morphine Equivalent Daily Dose

Table 4. Regression results, random sample of enrollees (N=1,000,000 people)[a]

	Any opioid use			MEDD>60			MEDD>120		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Guideline	0.845	(0.822, 0.868)	<0.001	0.946	(0.894, 1.006)	0.078	0.984	(0.893, 1.084)	0.741
Strong Policy	0.847	(0.818, 0.877)	<0.001	1.034	(0.962, 1.112)	0.367	1.033	(0.909 , 1.174)	0.623
Age	1.040	(1.039, 1.040)	<0.001	1.042	(1.040, 1.044)	<0.001	1.043	(1.040, 1.046)	<0.001
Male	0.848	(0.827, 0.870)	<0.001	0.916	(0.870, 0.963)	<0.001	0.944	(0.864, 1.032)	0.208
Months[b]	0.994	(0.994, 0.994)	<0.001	0.991	(0.990, 0.992)	<0.001	0.991	(0.989, 0.992)	<0.001

[a]Includes state fixed effects and clustering at the individual and state level

[b]Centered at January, 2012

Table 5. Summary of state-level regressions

	Guideline States		Strong Policy States	
Estimate and outcome	Range of estimates	Distribution of results[a]	Range of estimates	Distribution of results[a]
OR, any opioid use[b]	(0.67, 1.20)	1,3,0	(0.47, 1.05)	1,4,0
Change in MEDD[c]	(3.31, 8.2)	4,0,0	(-1.4, 5.5)	1,1,3
OR, dichotomous[c]	(1.04, 1.38)	4,0,0	(0.90, 1.28)	1,1,3
OR, excluded[d]	(1.04, 1.32)	4,0,0	(0.87, 1.23)	1,2,2
OR, targeted[d]	(1.01, 1.12)	3,0,0	(0.93, 1.30)	2,1,2

[a]Number of states with significant increases in MEDD, significant decreases in MEDD, and not statistically significant coefficients, respectively

[b]Random sample of one million enrollees from control and treatment states

[c]All opioid users from control and treatment states

[d]Using state-specific exclusions outlined in Table 1. South Carolina's policy had no exclusions, and is therefore not included in results.

Figures

Figure 1. Policy implementation timeline

	Policy	**2010**				**2011**				**2012**				**2013**				**2014**				**2015**			
AZ	Strong[a]																		X		X				
IN	Strong																				X				
RI	Strong																					X			
TN	Strong																			X					
WA	Strong[b]									X															
CA	Guideline																				X				
CO	Guideline																			X					
OH	Guideline														X										
SC	Guideline																				X				
VA	Control																								
WI	Control																								

[a]Had other policy (legislative act) and then guideline
[b]Had guideline prior to 2010 (2007) and other policy (legislative act) in 2012

Figure 2. Percent of random sample of enrollees with any opioid use, MEDD>120, and MEDD>60 (N=1,000,000 people)

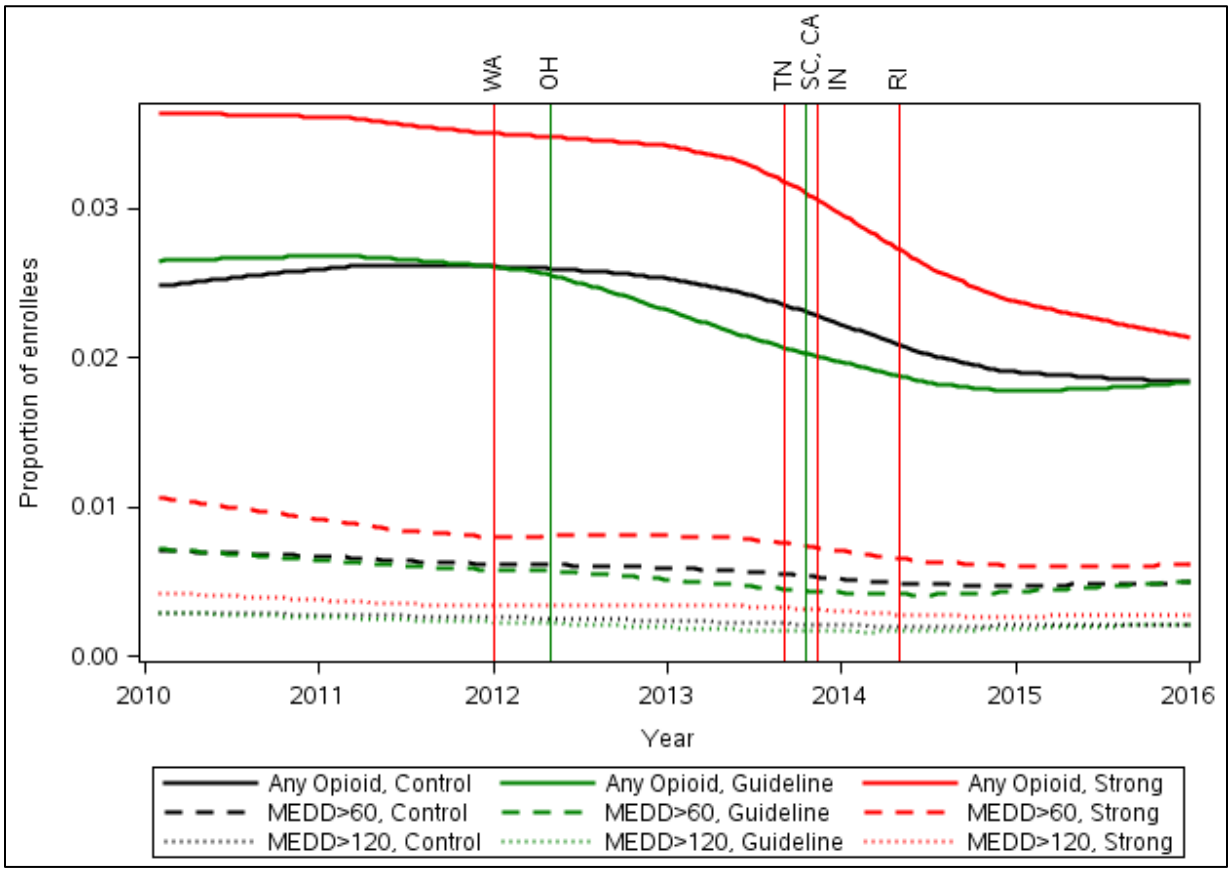
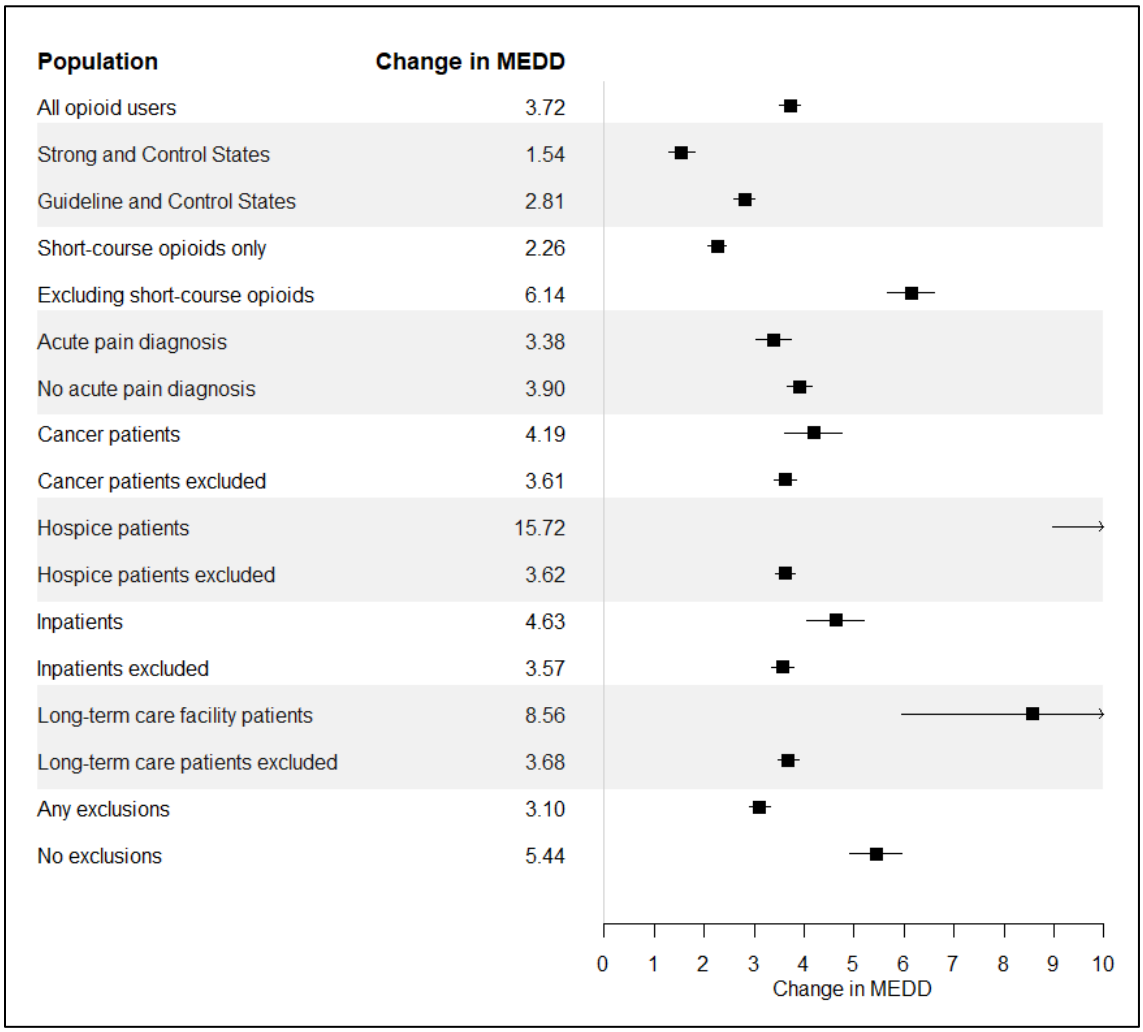


Figure 3. Summary of regression coefficients for any policy in effect in stratified analyses, restricted to opioid users



Appendix

Appendix 1. MarketScan quantity cleaning protocol

Relative frequencies of the quantity variable for prescription opioids was examined by year. Multiplier of ten quantity errors were present in all years, with errors more common beginning January, 2013. Frequencies of quantity were ranked pre- and post- 2013. Any quantity variable that, prior to 2013, was less frequent than the frequency of the quantity divided by ten was deemed to be incorrect. For example, 30 occurred more frequently than 300, so all 300 quantities were corrected to 30. The quantity 180, by contrast, occurred more frequently than the quantity 18 and was not corrected. The following values were corrected:

Original quantity variable	**Corrected quantity variable**
1-99, 101-121	No change
140, 150, 160, 200, 210, 280, 300, 350, 400, 450, 500, 560, 600, 750, 840, 900, 1200, 1800, 2400, 2700, 3600	Original quantity divided by 10
2000, 3000, 4000, 6000, 9000, 12000	Original quantity divided by 100
30000, 60000, 90000, 120000	Original quantity divided by 1000
300000, 600000, 900000, 1200000	Original quantity divide by 10,000
All other quantities <1000	No change
All other quantities ≥1000	Could not be determined, value designated missing

Figure 1. Mean MEDD by policy, opioid users only, with loess smoothing (smooth=0.4)

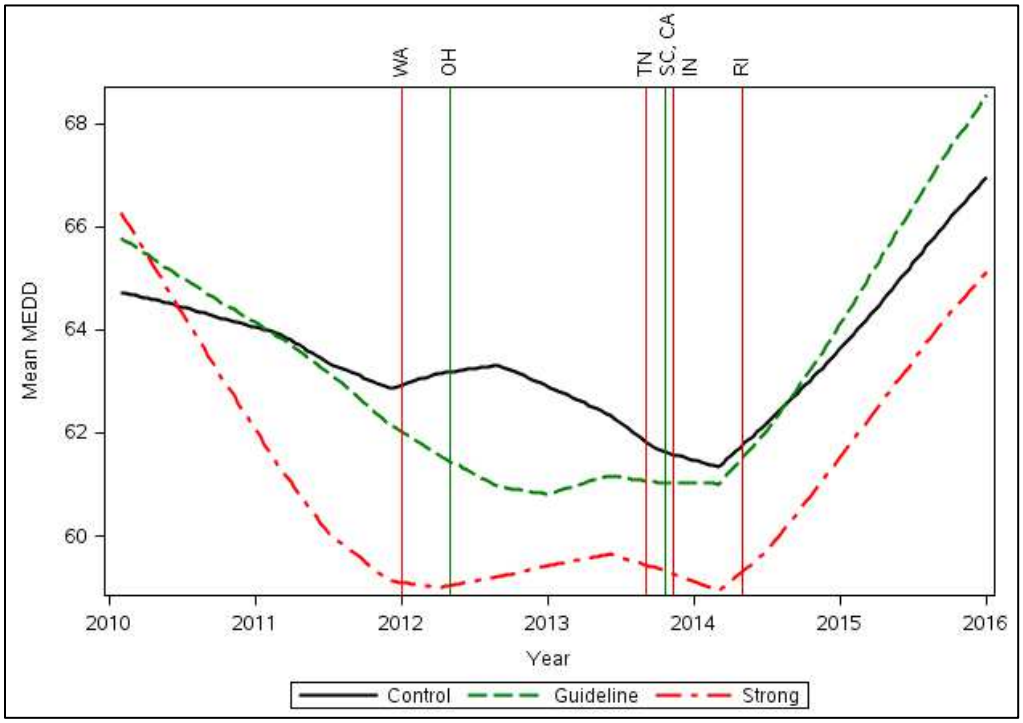


Figure 2. Log MEDD by policy, opioid users only, with loess smoothing (smooth=0.4)

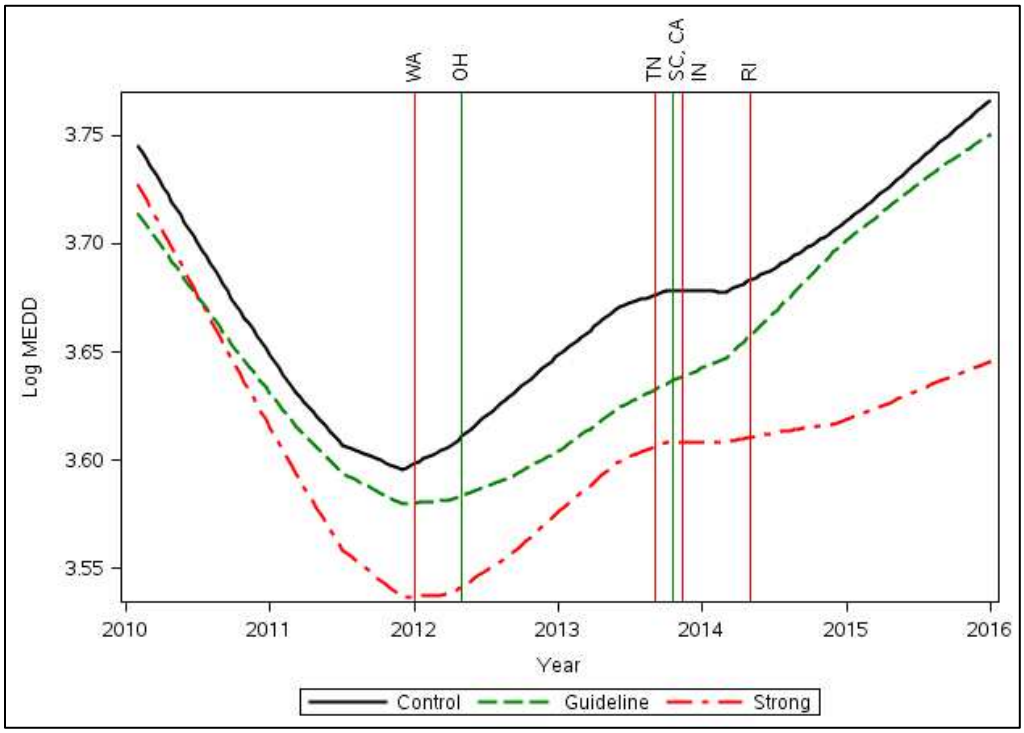


Figure 3. Proportion of opioid users with MEDD >120 by policy, opioid users only, with loess smoothing (smooth=0.4)

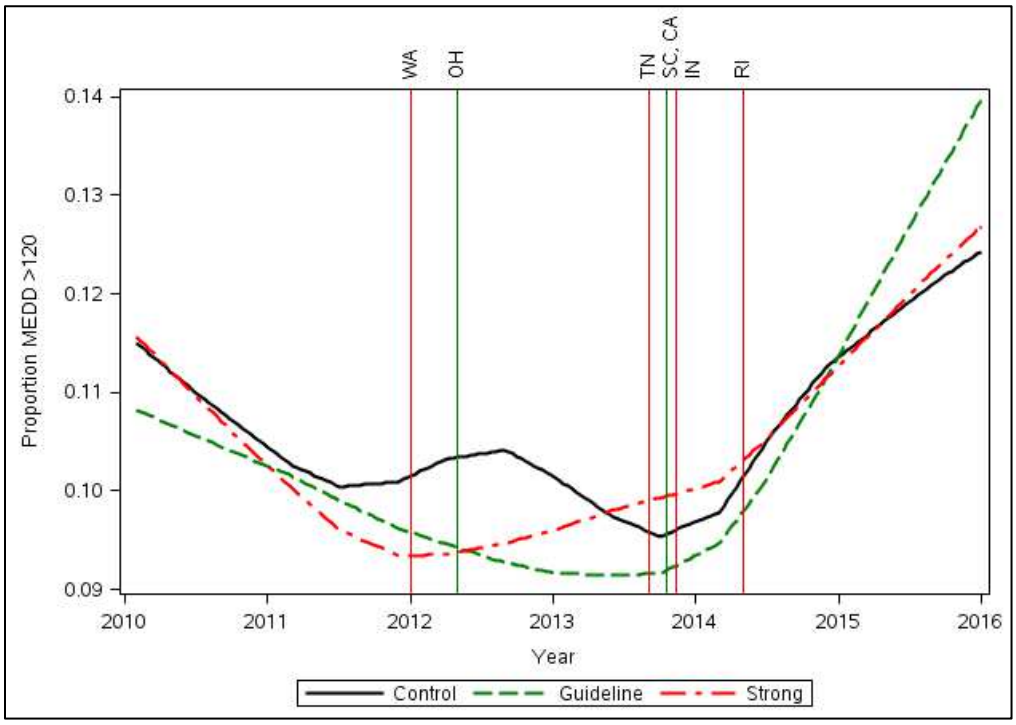


Figure 4. Proportion of individuals with MEDD >60 by policy, opioid users only, with loess smoothing (smooth=0.4)

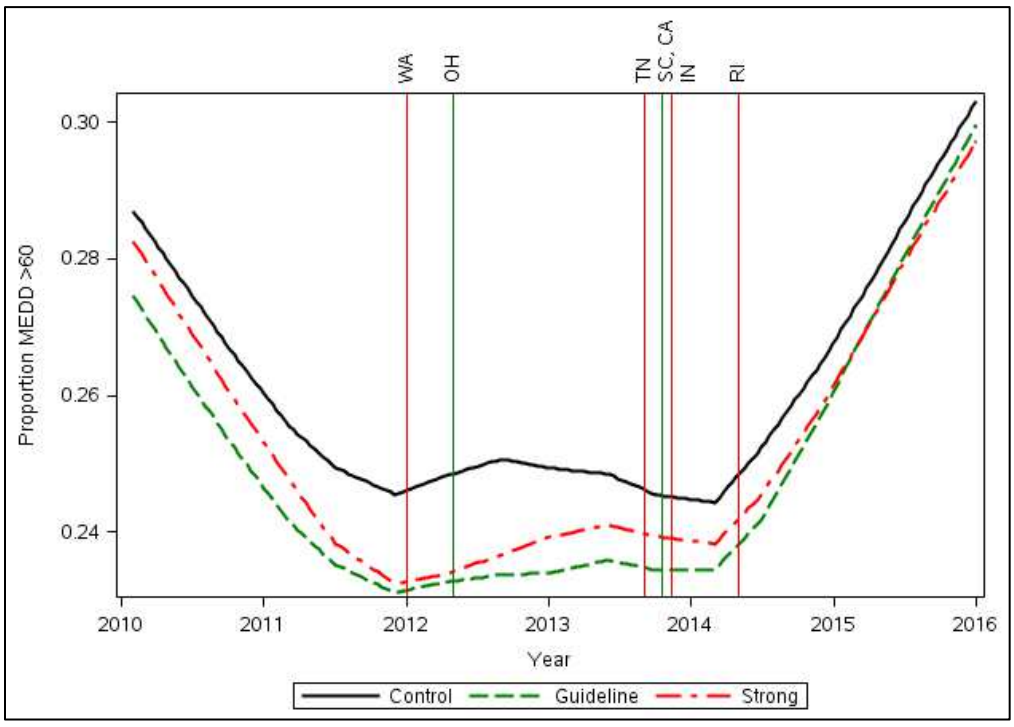


Table 1. Regression results, continuous MEDD outcome, any policy dichotomous, all patients (N=27,419,213 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.72	(3.51, 3.92)	<.001
Age	0.25	(0.24, 0.25)	<.001
Male	6.65	(6.56, 6.74)	<.001
Months after Jan 2010	-0.42	(-0.43, -0.42)	<.001
Months after Jan 2014	0.49	(0.47, 0.50)	<.001
Months since first opioid rx	0.63	(0.63, 0.63)	<.001

Table 2. Regression results, continuous MEDD outcome, any policy dichotomous, all states excluding Washington (N=26,008,150 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.76	(3.54, 3.97)	<.001
Age	0.25	(0.25, 0.26)	<.001
Male	6.74	(6.64, 6.83)	<.001
Months after Jan 2010	-0.43	(-0.43, -0.43)	<.001
Months after Jan 2014	0.50	(0.48, 0.51)	<.001
Months since first opioid rx	0.64	(0.63, 0.64)	<.001

Table 3. Regression results, logMEDD outcome, any policy dichotomous, all patients (N=27,409,820 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	0.02	(0.02, 0.02)	<.001
Age	0.00	(0.00, 0.00)	<.001
Male	0.06	(0.06, 0.06)	<.001
Months after Jan 2010	-0.00	(-0.00, -0.00)	<.001
Months after Jan 2014	0.01	(0.01, 0.01)	<.001
Months since first opioid rx	0.00	(0.00, 0.00)	<.001

Table 4. Regression results, continuous MEDD outcome, months policy in effect, all patients (N=27,419,213 person-months)

Variable	Estimate	95% CI	p-value
Months policy in effect	0.08	(0.07, 0.09)	<.001
Age	0.25	(0.24, 0.25)	<.001
Male	6.65	(6.56, 6.74)	<.001
Months after Jan 2010	-0.41	(-0.42, -0.41)	<.001
Months after Jan 2014	0.56	(0.55, 0.58)	<.001
Months since first opioid rx	0.63	(0.63, 0.63)	<.001

Table 5. Regression results, MEDD >120 outcome, any policy dichotomous, all patients (N=27,419,213 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	0.06	(0.06, 0.07)	<.001
Age	0.00	(0.00, 0.00)	<.001
Male	0.24	(0.24, 0.24)	<.001
Months after Jan 2010	-0.02	(-0.02, -0.02)	<.001
Months after Jan 2014	0.01	(0.01, 0.01)	<.001
Months since first opioid rx	0.03	(0.03, 0.03)	<.001

Table 6. Regression results, MEDD >100 outcome, any policy dichotomous, all patients (N=27,419,213 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	0.07	(0.06, 0.07)	<.001
Age	0.00	(0.00, 0.00)	<.001
Male	0.21	(0.21, 0.21)	<.001
Months after Jan 2010	-0.02	(-0.02, -0.02)	<.001
Months after Jan 2014	0.01	(0.01, 0.01)	<.001
Months since first opioid rx	0.03	(0.03, 0.03)	<.001

Table 7. Regression results, MEDD >80 outcome, any policy dichotomous, all patients (N=27,419,213 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	0.07	(0.07, 0.07)	<.001
Age	0.01	(0.01, 0.01)	<.001
Male	0.17	(0.17, 0.18)	<.001
Months after Jan 2010	-0.02	(-0.02, -0.02)	<.001
Months after Jan 2014	0.02	(0.02, 0.02)	<.001
Months since first opioid rx	0.02	(0.02, 0.02)	<.001

Table 8. Regression results, MEDD >60 outcome, any policy dichotomous, all patients (N=27,419,213 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	0.04	(0.04, 0.04)	<.001
Age	0.01	(0.00, 0.01)	<.001
Male	0.14	(0.14, 0.14)	<.001
Months after Jan 2010	-0.01	(-0.01, -0.01)	<.001
Months after Jan 2014	0.02	(0.02, 0.02)	<.001
Months since first opioid rx	0.01	(0.01, 0.02)	<.001

Table 9. Regression results, continuous MEDD outcome, dichotomous policies, strong policies and control states only (N=10,173,845 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	1.54	(1.28, 1.80)	<.001
Age	0.23	(0.22, 0.23)	<.001
Male	6.94	(6.82, 7.06)	<.001
Months after Jan 2010	-0.37	(-0.38, -0.37)	<.001
Months after Jan 2014	0.30	(0.29, 0.32)	<.001
Months since first opioid rx	0.59	(0.58, 0.59)	<.001

Table 10. Regression results, continuous MEDD outcome, dichotomous policies, guidelines and control states only (N=15,550,261 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	2.81	(2.59, 3.02)	<.001
Age	0.29	(0.28, 0.29)	<.001
Male	5.01	(4.91, 5.11)	<.001
Months after Jan 2010	-0.40	(-0.40, -0.39)	<.001
Months after Jan 2014	0.64	(0.62, 0.65)	<.001
Months since first opioid rx	0.61	(0.60, 0.61)	<.001

Table 11. Regression results, continuous MEDD outcome, any policy dichotomous, patients with high baseline use (>60 MEDD) (N=8,383,924 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	-1.18	(-1.95, -0.42)	0.003
Age	0.11	(0.10, 0.12)	<.001
Male	16.06	(15.80, 16.32)	<.001
Months after Jan 2010	-1.63	(-1.65, -1.60)	<.001
Months after Jan 2014	0.06	(0.01, 0.12)	0.017
Months since first opioid rx	1.66	(1.64, 1.68)	<.001

Table 12. Regression results, continuous MEDD outcome, any policy dichotomous, patients with no high baseline use (>60 MEDD) (N=10,977,814 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	-0.01	(-0.10, 0.09)	0.885
Age	-0.03	(-0.03, -0.03)	<.001
Male	0.86	(0.83, 0.89)	<.001
Months after Jan 2010	0.37	(0.36, 0.37)	<.001
Months after Jan 2014	0.15	(0.14, 0.15)	<.001
Months since first opioid rx	-0.14	(-0.14, -0.14)	<.001

Table 13. Regression results, continuous MEDD outcome, any policy dichotomous, patients with high baseline use (>80 MEDD) (N=6,153,112 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	-1.26	(-2.28, -0.24)	0.016
Age	0.12	(0.10, 0.13)	<.001
Male	19.99	(19.65, 20.34)	<.001
Months after Jan 2010	-1.55	(-1.58, -1.52)	<.001
Months after Jan 2014	-0.11	(-0.18, -0.04)	0.002
Months since first opioid rx	1.54	(1.51, 1.58)	<.001

Table 14. Regression results, continuous MEDD outcome, any policy dichotomous, patients with no high baseline use (>80 MEDD) (N=13,208,626 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	-0.14	(-0.24, -0.05)	0.003
Age	-0.03	(-0.03, -0.03)	<.001
Male	0.93	(0.90, 0.96)	<.001
Months after Jan 2010	0.30	(0.30, 0.31)	<.001
Months after Jan 2014	0.21	(0.21, 0.22)	<.001
Months since first opioid rx	-0.12	(-0.12, -0.11)	<.001

Table 15. Regression results, continuous MEDD outcome, any policy dichotomous, patients with high baseline use (>100) (N=4,536,037 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	-0.47	(-1.82, 0.89)	0.497
Age	0.27	(0.25, 0.29)	<.001
Male	23.22	(22.77, 23.68)	<.001
Months after Jan 2010	-1.25	(-1.30, -1.21)	<.001
Months after Jan 2014	-0.26	(-0.35, -0.17)	<.001
Months since first opioid rx	1.17	(1.13, 1.22)	<.001

Table 16. Regression results, continuous MEDD outcome, any policy dichotomous, patients with no high baseline use (>100) (N=14,825,701 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	-0.04	(-0.14, 0.06)	0.419
Age	-0.01	(-0.02, -0.01)	<.001
Male	1.05	(1.02, 1.08)	<.001
Months after Jan 2010	0.22	(0.22, 0.22)	<.001
Months after Jan 2014	0.29	(0.28, 0.30)	<.001
Months since first opioid rx	-0.08	(-0.08, -0.08)	<.001

Table 17. Regression results, continuous MEDD outcome, any policy dichotomous, patients with high baseline use (>120) (N=3,711,471 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	0.32	(-1.30, 1.94)	0.699
Age	0.41	(0.39, 0.44)	<.001
Male	24.52	(23.97, 25.08)	<.001
Months after Jan 2010	-1.08	(-1.14, -1.03)	<.001
Months after Jan 2014	-0.45	(-0.56, -0.34)	<.001
Months since first opioid rx	0.94	(0.89, 1.00)	<.001

Table 18. Regression results, continuous MEDD outcome, any policy dichotomous, patients with no high baseline use (>120) (N=15,650,267 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	-0.07	(-0.17, 0.03)	0.148
Age	-0.01	(-0.01, -0.00)	<.001
Male	1.09	(1.06, 1.13)	<.001
Months after Jan 2010	0.15	(0.15, 0.16)	<.001
Months after Jan 2014	0.32	(0.31, 0.33)	<.001
Months since first opioid rx	-0.03	(-0.03, -0.02)	<.001

Table 19. Regression results, continuous MEDD outcome, any policy dichotomous, short opioid courses only (N=17,544,583 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	2.26	(2.08, 2.43)	<.001
Age	0.19	(0.19, 0.19)	<.001
Male	2.00	(1.93, 2.08)	<.001
Months after Jan 2010	-0.22	(-0.22, -0.22)	<.001
Months after Jan 2014	0.41	(0.40, 0.42)	<.001
Months since first opioid rx	-0.07	(-0.07, -0.06)	<.001

Table 20. Regression results, continuous MEDD outcome, any policy dichotomous, excluding short opioid courses (N=9,874,630 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	6.14	(5.67, 6.60)	<.001
Age	-0.48	(-0.49, -0.47)	<.001
Male	11.59	(11.38, 11.80)	<.001
Months after Jan 2010	-0.53	(-0.54, -0.52)	<.001
Months after Jan 2014	1.03	(0.99, 1.06)	<.001
Months since first opioid rx	0.40	(0.39, 0.41)	<.001

Table 21. Regression results, continuous MEDD outcome, any policy dichotomous, acute patients only (N=9,040,356 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.38	(3.03, 3.73)	<.001
Age	0.39	(0.39, 0.40)	<.001
Male	5.56	(5.40, 5.72)	<.001
Months after Jan 2010	-0.42	(-0.43, -0.42)	<.001
Months after Jan 2014	0.51	(0.48, 0.53)	<.001
Months since first opioid rx	0.61	(0.60, 0.62)	<.001

Table 22. Regression results, continuous MEDD outcome, any policy dichotomous, excluding acute patients (N=18,378,857 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.90	(3.65, 4.16)	<.001
Age	0.16	(0.16, 0.17)	<.001
Male	7.37	(7.26, 7.48)	<.001
Months after Jan 2010	-0.43	(-0.43, -0.42)	<.001
Months after Jan 2014	0.48	(0.46, 0.49)	<.001
Months since first opioid rx	0.64	(0.64, 0.65)	<.001

Table 23. Regression results, continuous MEDD outcome, any policy dichotomous, cancer patients only (N=4,584,198 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	4.19	(3.61, 4.76)	<.001
Age	0.17	(0.16, 0.18)	<.001
Male	6.97	(6.71, 7.23)	<.001
Months after Jan 2010	-0.45	(-0.46, -0.44)	<.001
Months after Jan 2014	0.59	(0.55, 0.63)	<.001
Months since first opioid rx	0.57	(0.56, 0.58)	<.001

Table 24. Regression results, continuous MEDD outcome, any policy dichotomous, excluding cancer patients (N=22,835,015 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.61	(3.40, 3.83)	<.001
Age	0.24	(0.24, 0.24)	<.001
Male	6.73	(6.63, 6.83)	<.001
Months after Jan 2010	-0.42	(-0.42, -0.41)	<.001
Months after Jan 2014	0.47	(0.45, 0.48)	<.001
Months since first opioid rx	0.65	(0.64, 0.65)	<.001

Table 25. Regression results, continuous MEDD outcome, any policy dichotomous, hospice patients only (N=142,049 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	15.72	(8.96, 22.48)	<.001
Age	-1.16	(-1.33, -0.99)	<.001
Male	15.56	(12.69, 18.43)	<.001
Months after Jan 2010	-0.57	(-0.69, -0.44)	<.001
Months after Jan 2014	-0.14	(-0.63, 0.36)	0.589
Months since first opioid rx	1.23	(1.11, 1.36)	<.001

Table 26. Regression results, continuous MEDD outcome, any policy dichotomous, excluding hospice patients (N=27,277,164 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.62	(3.42, 3.82)	<.001
Age	0.23	(0.23, 0.24)	<.001
Male	6.58	(6.49, 6.67)	<.001
Months after Jan 2010	-0.42	(-0.43, -0.42)	<.001
Months after Jan 2014	0.49	(0.48, 0.51)	<.001
Months since first opioid rx	0.63	(0.63, 0.63)	<.001

Table 27. Regression results, continuous MEDD outcome, any policy dichotomous, inpatient only (N=4,575,387 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	4.63	(4.06, 5.20)	<.001
Age	0.28	(0.27, 0.29)	<.001
Male	9.76	(9.50, 10.02)	<.001
Months after Jan 2010	-0.51	(-0.52, -0.50)	<.001
Months after Jan 2014	0.49	(0.45, 0.53)	<.001
Months since first opioid rx	0.79	(0.78, 0.80)	<.001

Table 28. Regression results, continuous MEDD outcome, any policy dichotomous, excluding inpatient (N=22,843,826 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.57	(3.36, 3.79)	<.001
Age	0.21	(0.21, 0.21)	<.001
Male	6.56	(6.46, 6.66)	<.001
Months after Jan 2010	-0.40	(-0.41, -0.40)	<.001
Months after Jan 2014	0.46	(0.45, 0.48)	<.001
Months since first opioid rx	0.60	(0.60, 0.61)	<.001

Table 29. Regression results, continuous MEDD outcome, any policy dichotomous, long-term patients only (N=214,602 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	8.56	(5.95, 11.18)	<.001
Age	-1.00	(-1.09, -0.92)	<.001
Male	9.82	(8.58, 11.05)	<.001
Months after Jan 2010	-0.68	(-0.74, -0.63)	<.001
Months after Jan 2014	0.17	(-0.01, 0.36)	0.069
Months since first opioid rx	0.81	(0.76, 0.85)	<.001

Table 30. Regression results, continuous MEDD outcome, any policy dichotomous, excluding long-term patients (N=27,204,611 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.68	(3.48, 3.89)	<.001
Age	0.24	(0.24, 0.24)	<.001
Male	6.66	(6.57, 6.75)	<.001
Months after Jan 2010	-0.42	(-0.42, -0.42)	<.001
Months after Jan 2014	0.49	(0.47, 0.50)	<.001
Months since first opioid rx	0.63	(0.63, 0.63)	<.001

Table 31. Regression results, continuous MEDD outcome, any policy dichotomous, patients with any exclusions (N=20,377,456 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	3.10	(2.90, 3.31)	<.001
Age	0.32	(0.32, 0.32)	<.001
Male	3.39	(3.30, 3.48)	<.001
Months after Jan 2010	-0.33	(-0.33, -0.32)	<.001
Months after Jan 2014	0.40	(0.39, 0.42)	<.001
Months since first opioid rx	0.36	(0.35, 0.36)	<.001

Table 32. Regression results, continuous MEDD outcome, any policy dichotomous, patients with no exclusions (N=7,041,757 person-months)

Variable	Estimate	95% CI	p-value
Policy Dichotomous	5.44	(4.92, 5.95)	<.001
Age	-0.56	(-0.57, -0.55)	<.001
Male	11.51	(11.28, 11.74)	<.001
Months after Jan 2010	-0.49	(-0.50, -0.48)	<.001
Months after Jan 2014	1.00	(0.96, 1.04)	<.001
Months since first opioid rx	0.38	(0.37, 0.39)	<.001

Conclusion

Summary of Results and Future Work

Morphine Equivalent Daily Dose (MEDD) policies have been proposed as a tool for decreasing high dose prescribing, an important risk factor for opioid overdose. This dissertation examines the variation in state-level MEDD policies and evaluates their impact on prescribed dose in workers' compensation and privately insured populations.

In Chapter 2, state-level MEDD threshold policies were systematically identified and characterized on several categories including: state, agency/organization, policy type, effective date, threshold level, and policy exceptions. As of June 2017, 22 states had implemented 31 MEDD threshold policies, with several states implementing multiple policies. The most common type of policies were guidelines (14 states) followed by prior authorization requirements (4 states), rules/regulations (4 states), legislative acts (3 states), claim denials (2 states), and alert systems/automatic patient reports (2 states). There were a wide range of threshold values (30-300 mg MEDD) with threshold levels generally decreasing over time. The first types of policies implemented were most commonly guidelines while more restrictive types of policies, such as prior authorization and claim denial, were implemented in later years. Policies frequently recognized the need to exclude certain patient groups, most commonly patients with terminal illnesses or acute pain. Many policies allowed that dose thresholds may be exceeded if a pain specialist was consulted or prescribers made use of pain contracts or patient education.

In Chapter 3, two workers' compensation guidelines identified in Chapter 2 were evaluated using workers' compensation claims data from a large, national insurer. Both pre- and post-policy data were available for the guideline states—Massachusetts and Connecticut—as well as three control states allowing for an interrupted time series with comparison states design. Guideline passage was associated with an 11% decrease in prescribed MEDD and larger decreases were observed in claimants with chronic, non-cancer pain and high dose opioid use at baseline. Larger decreases were also seen in Massachusetts as compared to Connecticut, possibly due to differences in dissemination.

In Chapter 4, additional policies identified in Chapter 2, comprised of guidelines, rules/regulations, legislative acts, and passive alert systems, were evaluated using a large, nationally representative sample of commercial claims data. An interrupted time series with comparison states design was employed with opioid utilization outcomes. Additional stratified analyses conducted among opioid users examined each state policy individually and evaluated the policies separately by groups explicitly excluded by the policies (patients with cancer, acute pain diagnoses, hospice, inpatient or long-term care facility use and short courses of opioids) to determine if the policies were being targeted as intended. Policy implementation was associated with 15% lower odds of any opioid use among enrollees, but no significant change in the odds of receiving high dose prescriptions, specifically. In the population of opioid users, there was actually a small increase in prescribed dose. Furthermore, changes in opioid use did not appear to be targeted towards intended groups of patients with increased MEDD associated with policy passage relative to control states across all excluded and targeted groups.

Overall, a major finding of this study is that states have implemented a number of MEDD threshold policies, but there is no consensus as to how these policies should be structured. In the context of a workers' compensation population, passage of MEDD threshold guidelines was associated with a decrease in prescribed MEDD. However, passage of MEDD threshold policies was not associated with a decrease in prescribed MEDD in a privately insured population. It is possible that guidelines targeted towards a specific population, e.g., injured workers, may be more effective than those aimed at the general population. This work builds on previous work by comprehensively identifying and characterizing MEDD threshold policies and by evaluating these types of policies in states outside of Washington and in privately insured populations.

As a whole, this research had a number of important strengths. Chapter 2 provided a systematic review of state-level MEDD policies and characterized several important aspects of these policies, including sponsoring agency, date implemented, and excluded patient groups. This research laid the groundwork for the evaluations of MEDD policies conducted in Chapters 3 and 4, as well as for future research on additional state-level MEDD policies. For example, the results of Chapter 2 informed the selection of control and treatment states in Chapters 3 and 4 as well as sensitivity analyses stratifying by relevant clinical subgroups. The evaluations in Chapters 3 and 4 also made use of sizeable patient populations with longitudinal data from multiple states. This data allowed for an interrupted time series with a comparison group study design, a superior design to previous evaluations which did not utilize comparison states.

This research also had a number of important limitations. Chapter 2 did not systematically examine policies at the national or local level, which may have a great influence on prescribing

behavior. Certain policy characteristics, such as dissemination and enforcement efforts, were not systematically collected and limit the conclusions that may be drawn about the changes in prescribing observed in Chapters 3 and 4. Claims data were used to evaluate a subset of policies and these data include several important limitations. Namely, these data only contain information on opioids obtained through the insurer and lack information on pain ratings and detailed medical history. The evaluations of MEDD policy in Chapters 3 and 4 must also be interpreted in light of the complex and rapidly changing policy environment surrounding opioids in the years since Washington implemented its MEDD guidelines in 2007. While careful selection of treatment and control states mitigated some historical threats to the study, policy changes at the local or individual insurer level may have influenced MEDD in ways that were not taken into account. The generalizability of these evaluations should also be taken into consideration. In particular, the evaluation of workers' compensation policies only examined two states and one workers' compensation insurer.

Future work should seek to determine why MEDD threshold policies may work in some contexts, but not others and examine the impact of MEDD threshold policies in other populations, including impacts on patient health outcomes. This may include surveys or qualitative work understanding how policies influence prescriber behavior in practice. For example, a survey of prescribers in states which passed guidelines evaluating their knowledge of the guidelines could help illustrate the mechanisms through which guidelines influence (or fail to influence) prescriber behavior.

MEDD policies should also be evaluated in other contexts and populations. In particular, data were not available for this study to evaluate the impact of prior authorization or claim denial MEDD policies, which may have a greater impact on prescribing behavior than the other types of policies studied—namely guidelines, rules/regulations, legislation, and automatic alerts/patient reports. For example, Medicaid has implemented prior authorization and claim denial based on MEDD. The impact of MEDD policies on patient outcomes is also important, particularly among policies that were shown to be associated with changes in provider behavior.

Future research should also investigate whether reducing prescribed dose has any unintended consequences. One unintended consequence of concern is that patients who would have otherwise received high doses of opioids may not be receiving adequate pain treatment or may experience withdrawal symptoms leading to the use of heroin or other illegal sources of opioid drugs. Better understanding these pathways of opioid use and developing adequate support for patients to manage their pain through other means such as cognitive behavioral therapy or non-opioid medications should be a research priority.

Policy, Practice, and Research Implications

For policymakers interested in implementing MEDD threshold policies, there are a number of different options from guidelines to legislative acts to prior authorization requirements to consider. The compendium of policies presented in Chapter 2 will allow policymakers to review what has been done in other states and highlights important patient groups that should be considered for exclusion.

Disseminating MEDD guidelines to doctors who treat workers' compensation cases may reduce high-dose opioid prescribing: an important risk factor for opioid-related mortality, while still allowing for autonomy in practice. Critically, MEDD guidelines would allow prescribers to use their clinical judgment to incorporate differences in drug formulations and individual pain management needs into their prescribing decisions. However, better understanding of MEDD, its calculation, and its limitations is necessary for these types of policies to have a positive impact. There are a growing number of resources available for providers to determine the overall MEDD prescribed to patients, such as online opioid calculators, but only a small number of policies automatically calculate MEDD and take into account multiple and overlapping prescriptions (e.g., states with alert systems/automatic reports). Improving provider education surrounding MEDD measurement and reducing the burden on providers to make these calculations and keep track of multiple prescriptions may be an important first step.

As policymakers seek to adopt new prescribing guidelines, it is important to recognize that high-dose opioid prescribing is only one risk factor for opioid mortality and a multi-pronged strategy that takes other risk factors into account, such as opioid diversion, days supply of drugs, and co-use of other drugs such as alcohol or benzodiazepines, may be more appropriate. Critically, follow-up with patients who have tapered from high-dose prescribing is needed to ensure that these patients do not turn to other sources of drugs and receive adequate support managing their pain.

Researchers may use the results of Chapter 2 to inform future evaluations of state-level MEDD policies. In particular, Medicaid policies and policies implemented after 2015 should be evaluated and compared to the results of Chapters 3 and 4. The claims-based methods of

evaluation used in Chapters 3 and 4 can also be used in future claims-based evaluations of MEDD policies and are an important contribution to the literature.

References

1. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA J Am Med Assoc*. 2008;300(22):2613-2620.

2. Centers for Disease Control. Injury Prevention and Control: Data and Statistics. 2015. http://www.cdc.gov/injury/wisqars/.

3. Abuse NI on D. Overdose Death Rates. https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates. Published September 15, 2017. Accessed March 31, 2018.

4. Crane EH. Emergency department visits involving narcotic pain relievers. Drug Abuse Warning Network. 2015.

5. Center for Behavioral Health Statistics and Quality. Results from the 2014 national survey on drug use and health: Detailed tables. http://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs2014/NSDUH-DetTabs2014.pdf. Accessed September 14, 2016.

6. Centers for Disease Control and Prevention (CDC). Vital signs: overdoses of prescription opioid pain relievers---United States, 1999--2008. *MMWRMorbidity Mortal Wkly Rep*. 2011;60(43):1487-1492. doi:mm6043a4 [pii]

7. Centers for Disease Control. 10 Leading Causes of Death, United States 2013-2014. http://www.cdc.gov/injury/images/lc-charts/leading_causes_of_death_by_age_group_2013-a.gif.

8. Centers for Disease Control. FastStats. http://www.cdc.gov/nchs/fastats/accidental-injury.htm. Accessed September 14, 2016.

9. Paulozzi LJ, Kilbourne EM, Shah NG, et al. A history of being prescribed controlled substances and risk of drug overdose death. *Pain Med Malden Mass*. 2012;13(1):87-95. doi:10.1111/j.1526-4637.2011.01260.x

10. Rosenblum A, Marsch LA, Joseph H, Portenoy RK. Opioids and the treatment of chronic pain: controversies, current status, and future directions. *Exp Clin Psychopharmacol*. 2008;16(5):405.

11. King LS. The American Disease: Origins of Narcotic Control. *JAMA*. 1973;225(3):316-316.

12. Pasero CL, McCaffery M. Pain ratings: the fifth vital sign. *AJN Am J Nurs*. 1997;97(2):15.

13. Morrison RS, Magaziner J, McLaughlin MA, et al. The impact of post-operative pain on outcomes following hip fracture. *Pain*. 2003;103(3):303-311.

14. Eccleston C, Crombez G. Pain demands attention: A cognitive–affective model of the interruptive function of pain. *Psychol Bull*. 1999;125(3):356.

15. Paulozzi LJ, Weisler RH, Patkar AA. A national epidemic of unintentional prescription opioid overdose deaths: how physicians can help control it. *J Clin Psychiatry*. 2011;72(5):589-592. doi:10.4088/JCP.10com06560

16. Von Korff MR, Franklin G. Responding to America's Iatrogenic Epidemic of Prescription Opioid Addiction and Overdose. *Med Care*. 2016;54(5):426-429.

17. Fillingim RB. Sex, gender, and pain: women and men really are different. *Curr Pain Headache Rep*. 2000;4(1):24-30.

18. Gove WR. Gender differences in mental and physical illness: The effects of fixed roles and nurturant roles. *Soc Sci Med*. 1984;19(2):77-84. doi:10.1016/0277-9536(84)90273-9

19. Paulozzi LJ, Strickler GK, Kreiner PW, Koris CM. Controlled substance prescribing patterns—prescription behavior surveillance system, eight states, 2013. *MMWR Surveill Summ*. 2015;64(9):1-14.

20. Liu Y, Logan JE, Paulozzi LJ, Zhang K, Jones CM. Potential misuse and inappropriate prescription practices involving opioid analgesics. *Am J Manag Care*. 2013;19(8):648-665. doi:85159 [pii]

21. Becker WC, Sullivan LE, Tetrault JM, Desai RA, Fiellin DA. Non-medical use, abuse and dependence on prescription opioids among U.S. adults: Psychiatric, medical and substance use correlates. *Drug Alcohol Depend*. 2008;94(1–3):38-47. doi:10.1016/j.drugalcdep.2007.09.018

22. Chen L, Hedegaard H, Warner M. Drug-poisoning Deaths Involving Opioid Analgesics: United States, 1999-2011. *NCHS Data Brief*. 2014;(166):1-8.

23. Paulozzi LJ, Xi Y. Recent changes in drug poisoning mortality in the United States by urban–rural status and by drug type. *Pharmacoepidemiol Drug Saf*. 2008;17(10):997-1005.

24. Cicero TJ, Surratt H, Inciardi JA, Munoz A. Relationship between therapeutic use and abuse of opioid analgesics in rural, suburban, and urban locations in the United States. *Pharmacoepidemiol Drug Saf*. 2007;16(8):827-840.

25. Dick AW, Pacula RL, Gordon AJ, et al. Growth In Buprenorphine Waivers For Physicians Increased Potential Access To Opioid Agonist Treatment, 2002-11. *Health Aff Proj Hope*. 2015;34(6):1028-1034. doi:10.1377/hlthaff.2014.1205

26. Rosenblatt RA, Andrilla CHA, Catlin M, Larson EH. Geographic and specialty distribution of US physicians trained to treat opioid use disorder. *Ann Fam Med*. 2015;13(1):23-26. doi:10.1370/afm.1735

27. Reid MC, Engles-Horton LL, Weber MB, Kerns RD, Rogers EL, O'Connor PG. Use of opioid medications for chronic noncancer pain syndromes in primary care. *J Gen Intern Med*. 2002;17(3):173-179.

28. Magni G, Moreschi C, Rigatti-Luchini S, Merskey H. Prospective study on the relationship between depressive symptoms and chronic musculoskeletal pain. *Pain*. 1994;56(3):289-297.

29. Castillo RC, Wegener ST, Heins SE, Haythornthwaite JA, MacKenzie EJ, Bosse MJ. Longitudinal Relationships between Anxiety, Depression, and Pain: Results from a Two Year Cohort Study of Lower Extremity Trauma Patients. *Pain*. 2013;(Journal Article).

30. Franklin GM, Stover BD, Turner JA, Fulton-Kehoe D, Wickizer TM. Early opioid prescription and subsequent disability among workers with back injuries: the Disability Risk Identification Study Cohort. *Spine*. 2008;33(2):199.

31. Webster BS, Verma SK, Gatchel RJ. Relationship between early opioid prescribing for acute occupational low back pain and disability duration, medical costs, subsequent surgery and late opioid use. *Spine*. 2007;32(19):2127.

32. Heins SE, Feldman DR, Bodycombe D, Wegener ST, Castillo RC. Early opioid prescription and risk of long-term opioid use among US workers with back and shoulder injuries: a retrospective cohort study. *Inj Prev J Int Soc Child Adolesc Inj Prev*. 2015;(Journal Article). doi:injuryprev-2015-041630 [pii]

33. Kraut A, Shafer LA, Raymond CB. Proportion of opioid use due to compensated workers' compensation claims in Manitoba, Canada. *Am J Ind Med*. 2015;58(1):33-39.

34. Peirce GL, Smith MJ, Abate MA, Halverson J. Doctor and Pharmacy Shopping for Controlled Substances: *Med Care*. 2012;50(6):494-500. doi:10.1097/MLR.0b013e31824ebd81

35. Clark T, Eadie J, Kreiner P, Strickler G. Prescription Drug Monitoring Programs. 2012;(Journal Article).

36. Thomas CP, Kim M, Nikitin RV, Kreiner P, Clark TW, Carrow GM. Prescriber response to unsolicited prescription drug monitoring program reports in Massachusetts. *Pharmacoepidemiol Drug Saf*. 2014;23(9):950-957.

37. Okie S. A flood of opioids, a rising tide of deaths. *N Engl J Med*. 2010;363(21):1981-1985.

38. Coplan PM, Kale H, Sandstrom L, Landau C, Chilcoat HD. Changes in oxycodone and heroin exposures in the National Poison Data System after introduction of extended-release oxycodone with abuse-deterrent characteristics. *Pharmacoepidemiol Drug Saf*. 2013;22(12):1274-1282.

39. Harris SC, Perrino PJ, Smith I, et al. Abuse potential, pharmacokinetics, pharmacodynamics, and safety of intranasally administered crushed oxycodone HCl abuse-deterrent controlled-release tablets in recreational opioid users. *J Clin Pharmacol*. 2014;54(4):468-477.

40. Vosburg SK, Jones JD, Manubay JM, Ashworth JB, Benedek IH, Comer SD. Assessment of a formulation designed to be crush-resistant in prescription opioid abusers. *Drug Alcohol Depend*. 2012;126(1):206-215.

41. Vosburg SK, Jones JD, Manubay JM, Ashworth JB, Shapiro DY, Comer SD. A comparison among tapentadol tamper-resistant formulations (TRF) and OxyContin®(non-TRF) in prescription opioid abusers. *Addiction*. 2013;108(6):1095-1106.

42. Haegerich TM, Paulozzi LJ, Manns BJ, Jones CM. What we know, and don't know, about the impact of state policy and systems-level interventions on prescription drug overdose. *Drug Alcohol Depend*. 2014;145(Journal Article):34-47.

43. Ripamonti C, Groff L, Brunelli C, Polastri D, Stavrakis A, De Conno F. Switching from morphine to oral methadone in treating cancer pain: what is the equianalgesic dose ratio? *J Clin Oncol Off J Am Soc Clin Oncol*. 1998;16(10):3216-3221.

44. California Department of Health. Clinical Review: Morphine Equivalent Daily Dose to Prevent Opioid Overuse. 2014. https://files.medi-cal.ca.gov/pubsdoco/dur/Articles/dured_24035.pdf.

45. Tennessee Department of Health. Chronic Pain Guidelines. https://www.tn.gov/assets/entities/health/attachments/ChronicPainGuidelines.pdf. Accessed September 7, 2016.

46. Prescription Drug Monitoring Program Center of Excellence at Brandeis. *Options for Unsolicited Reporting*. 2015.

47. American College of Occupational Medicine. *Occupational Medicine Practice Guidelines: Evaluation and Management of Common Health Problems and Functional Recovery of Workers*. Vol 3. Beverly Farms: OEM Press; 2008.

48. Work Loss Institute. *Official Disability Guidelines*. Vol 16. Encinitas, CA: Work Loss Data Institute; 2011.

49. California Division of Workers Compensation. Proposed Opioid Treatment Guidelines MTUS, 8. C.C.R. §9792.24.4. July 2015. http://www.dir.ca.gov/dwc/DWCPropRegs/MTUS-Opioids-ChronicPain/Opioids-Guidelines.pdf.

50. Ohio Bureau of Workers Compensation. Opioid Prescribing Guidelines. 2016. https://www.bwc.ohio.gov/provider/brochureware/OpioidEducate/default.asp. Accessed April 10, 2018.

51. Commonwealth of Massachusetts Department of Industrial Accidents. Chronic Pain Treatment Guidelines. February 2012. http://www.mass.gov/lwd/workers-compensation/hcsb/tg/chronic-pain-treatment-guideline.pdf.

52. Control C for D, Prevention USD of H Public Health Service, Services H. Guideline for Prescribing Opioids for Chronic Pain. *J Pain Palliat Care Pharmacother*. 2016;30(2):138-140. doi:10.3109/15360288.2016.1173761

53. Rennick A, Atkinson T, Cimino NM, Strassels SA, McPherson ML, Fudin J. Variability in Opioid Equivalence Calculations. *Pain Med*. 2016;17(5):892-898. doi:10.1111/pme.12920

54. Ziegler SJ. The Proliferation of Dosage Thresholds in Opioid Prescribing Policies and Their Potential to Increase Pain and Opioid-Related Mortality. *Pain Med*. 2015;16(10):1851-1856.

55. Unintended Harm from Opioid Prescribing Guidelines - Fishman - 2009 - Pain Medicine - Wiley Online Library. http://onlinelibrary.wiley.com/doi/10.1111/j.1526-4637.2008.00553.x/abstract. Accessed October 9, 2017.

56. Franklin GM, Mai J, Turner J, Sullivan M, Wickizer T, Fulton-Kehoe D. Bending the prescription opioid dosing and mortality curves: impact of the Washington State opioid dosing guideline. *Am J Ind Med*. 2012;55(4):325-331.

57. Sullivan MD, Bauer AM, Fulton-Kehoe D, et al. Trends in Opioid Dosing Among of Washington State Medicaid Patients Before and After Opioid Dosing Guideline Implementation. *J Pain*. 2016;(Journal Article).

58. Kooij FO, Klok T, Hollmann MW, Kal JE. Decision Support Increases Guideline Adherence for Prescribing Postoperative Nausea and Vomiting Prophylaxis: *Anesth Analg*. 2008;106(3):893-898. doi:10.1213/ane.0b013e31816194fb

59. Tooher R, Middleton P, Pham C, et al. A Systematic Review of Strategies to Improve Prophylaxis for Venous Thromboembolism in Hospitals. *Ann Surg*. 2005;241(3):397-415.

60. Abraham NS, El–Serag HB, Johnson ML, et al. National Adherence to Evidence-Based Guidelines for the Prescription of Nonsteroidal Anti-Inflammatory Drugs. *Gastroenterology*. 2005;129(4):1171-1178. doi:10.1053/j.gastro.2005.08.003

61. Weinmann S, Janssen B, Gaebel W. Guideline adherence in medication management of psychotic disorders: an observational multisite hospital study. *Acta Psychiatr Scand*. 2005;112(1):18-25. doi:10.1111/j.1600-0447.2005.00547.x

62. Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. *BMJ*. 2005;330(7494):765. doi:10.1136/bmj.38398.500764.8F

63. Eslami S, Keizer NF de, Abu-Hanna A. The impact of computerized physician medication order entry in hospitalized patients—A systematic review. *Int J Med Inf*. 2008;77(6):365-376. doi:10.1016/j.ijmedinf.2007.10.001

64. Donabedian A. The quality of care: How can it be assessed? *Jama*. 1988;260(12):1743-1748.

65. O'Donnell JK. Trends in Deaths Involving Heroin and Synthetic Opioids Excluding Methadone, and Law Enforcement Drug Product Reports, by Census Region — United States, 2006–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66. doi:10.15585/mmwr.mm6634a2

66. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med*. 2010;152(2):85-92.

67. Bohnert ASB, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA J Am Med Assoc*. 2011;305(13):1315-1321.

68. Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN. Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med*. 2011;171(7):686-691.

69. Washington Department of Labor and Industries. Interim Evaluation of the Washington State Interagency Guideline on Opioid Dosing for Chronic Non-Cancer Pain. 2009. http://www.agencymeddirectors.wa.gov/files/agreportfinal.pdf.

70. Fulton-Kehoe D, Garg RK, Turner JA, et al. Opioid poisonings and opioid adverse effects in workers in Washington State. *Am J Ind Med*. 2013;56(12):1452-1462.

71. Fulton-Kehoe D, Sullivan MD, Turner JA, et al. Opioid poisonings in Washington State Medicaid: trends, dosing, and guidelines. *Med Care*. 2015;53(8):679-685. doi:10.1097/MLR.0000000000000384

72. Agency for Healthcare Research and Quality. National Guideline Clearinghouse. 2016. http://www.guideline.gov/index.aspx.

73. The National Alliance for Model State Drug Laws (NAMSDL). http://www.namsdl.org/. Accessed October 23, 2017.

74. Pain & Policy Studies Group. *Profiles of State Policies Governing Drug Control and Medical and Pharmacy Practice*. University of Wisconsin; 2015.

75. Center for Medicare and Medicaid Services. *Medicaid Drug Utilization Review State Comparison/Summary Report FFY 2015 Annual Report*.; 2016.

76. Officer EDTPCT. Curbing Prescription Drug Abuse With Patient Review and Restriction Programs. http://pew.org/1q69pHC. Accessed September 6, 2017.

77. Insurance TD of. *Pharmacy Closed Rule Development and Implementation*. Vol 2016.; 2016.

78. Riggs CS, Billups SJ, Flores S, Patel RJ, Heilmann RMF, Milchak JL. Opioid Use for Pain Management After Implementation of a Medicaid Short-Acting Opioid Quantity Limit. *J Manag Care Spec Pharm*. 2017;23(3):346-354. doi:10.18553/jmcp.2017.23.3.346

79. New Prescribing Law For Treatment of Acute and Chronic Pain | NJAFP. https://www.njafp.org/content/new-prescribing-law-treatment-acute-and-chronic-pain. Accessed November 27, 2017.

80. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA*. 2016.

81. Fulton-Kehoe D, Garg RK, Turner JA, et al. Opioid poisonings and opioid adverse effects in workers in Washington State. *Am J Ind Med*. 2013;56(12):1452-1462.

82. Roberts ET, DuGoff EH, Heins SE, et al. Evaluating Clinical Practice Guidelines Based on Their Association with Return to Work in Administrative Claims Data. *Health Serv Res*. 2015;(Journal Article).

83. Trujillo AJ, Heins SE, Anderson GF, Castillo RC. Geographic variability of adherence to occupational injury treatment guidelines. *J Occup Environ Med Am Coll Occup Environ Med*. 2014;56(12):1308-1312. doi:10.1097/JOM.0000000000000264

84. Buttorff C, Trujillo AJ, Castillo R, Vecino-Ortiz AI, Anderson GF. The impact of practice guidelines on opioid utilization for injured workers. *Am J Ind Med*. 2017;60(12):1023-1030. doi:10.1002/ajim.22779

85. Mack KA, Zhang K, Paulozzi L, Jones C. Prescription practices involving opioid analgesics among Americans with Medicaid, 2010. *J Health Care Poor Underserved*. 2015;26(1):182-198. doi:10.1353/hpu.2015.0009 [doi]

86. Clark DE, Osler TM, Hahn DR. *ICDPIC*.; 2009.

87. Kennedy-Hendricks A, Richey M, McGinty EE, Stuart EA, Barry CL, Webster DW. Opioid overdose deaths and Florida's crackdown on pill mills. *Am J Public Health*. 2016;(0):e1-e8.

88. Dasgupta N, Creppage K, Austin A, Ringwalt C, Sanford C, Proescholdbell SK. Observed Transition from Opioid Analgesic Deaths towards Heroin. *Drug Alcohol Depend*. 2014.

89. Alpert A, Powell D, Pacula RL. *Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids*. National Bureau of Economic Research; 2017. doi:10.3386/w23031

90. Paulozzi LJ, Zhang K, Jones CM, Mack KA. Risk of adverse health outcomes with increasing duration and regularity of opioid therapy. *J Am Board Fam Med JABFM*. 2014;27(3):329-338. doi:10.3122/jabfm.2014.03.130290

91. Truven Health Analytics. Truven Health MarketScan Research Databases. 2012.

92. Centers for Disease Control Injury Center. Data Resources, Analyzing Prescription Data and Morphine Milligram Equivalents (MME). https://www.cdc.gov/drugoverdose/resources/data.html. 2017.

Curriculum Vitae

Sara E. Heins

508 Hampton House, Department of Health Policy and Management
Johns Hopkins Bloomberg School of Public Health
Phone: 517-282-5255
sheins2@jhu.edu

EDUCATION

PhD Student, Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD (May 2018, Anticipated)
Concentration: Health Services Research
Certificate Program: Injury and Violence Prevention

B.A, Biology and Society, *Magna Cum Laude*, Cornell University, Ithaca, NY (2011)
Minors: Global Health, Southeast Asian Studies

PROFESSIONAL EXPERIENCE

2018-Present: Health Policy Researcher, RAND Corporation, Pittsburgh, PA

2015-2018: Student Research Assistant, Outcomes after Critical Care and Surgery group, Department of Pulmonary and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, MD

2016-2018: Adjunct Researcher, RAND Corporation, Pittsburgh, PA

2014-2016: Student Research Assistant, Center for Population Health and Information Technology, Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Summer 2016: Summer Associate, RAND Corporation, Pittsburgh, PA

2013-2014: Sr. Research Assistant/Programmer, Major Extremity Trauma Research Consortium, Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

2011- 2013: Research Assistant/Programmer, Center for Injury Research and Policy, Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

2009-2011: Research Assistant, Department of Plant Pathology, Cornell University, Ithaca, NY

TEACHING EXPERIENCE

Spring, 2018: Primary Instructor (Gordis Teaching Fellowship), Using Secondary Data for Public Health Research, Johns Hopkins University

Spring, 2016 and 2017: Teaching Assistant, Managed Care and Health Insurance, Johns Hopkins Bloomberg School of Public Health

Fall 2016: Teaching Assistant, Health Economics I, Johns Hopkins Bloomberg School of Public Health

Fall, 2015 and 2016: Teaching Assistant, Quality of Medical Care, Johns Hopkins Bloomberg School of Public Health

Spring, 2015: Teaching Assistant, Research and Evaluation Methods for Health Policy I-II, Johns Hopkins Bloomberg School of Public Health

Spring, 2014: Teaching Assistant, Introduction to Health Services Research and Evaluation, Johns Hopkins Bloomberg School of Public Health

MENTORING AND VOLUNTEER EXPERIENCE

2014-Present: President (2015-Present), Healthy Minds Math Teaching and Mentoring Program, Commodore John Rogers Elementary and Middle School, Baltimore, MD

2013-Present: Cornell Global Health Mentor, Cornell University

2013-Present: Cornell Alumni Admissions Ambassador, Cornell Alumni Admissions Ambassador Network

2010-2011: Campus Ambassador, CET Academic Programs

2010: Volunteer, Little Rose Shelter for Teenage Girls, Ho Chi Minh City, Vietnam

PROFESSIONAL ACTIVITIES

2017: American Public Health Association, Student Member
2017: International Society for Pharmacoeconomics and Outcomes Research, Student Member
2014-2017: Society for Advancement of Violence and Injury Research, Student Member
2014-2017: AcademyHealth, Student Member

EDITORIAL ACTIVITIES

2016: Referee, BMJ Open

AWARDS AND HONORS

- R36 Dissertation Award, Agency for Healthcare Quality and Research, 2017-2018
- Gordis Teaching Fellowship recipient, 2016
- Manuscript "Distinctive injury deaths: The role of environment, policy, and measurement across states" selected for US Focus media promotion by BMJ Journals, 2015
- Passed PhD Qualifying Exam with Honors, 2015
- SAVIR Student Paper Award, 2015
- NIOSH ERC Training Grant 2014-2017
- Biology and Society Honors Program, Cornell University, 2010-2011
- Dean's List, Cornell University, 2010-2011
- USCA Academic All-American, Cross-Country Skiing, 2011
- Teagle Foundation Scholarship Recipient, 2007-2011
- National Multiple Sclerosis Foundation Scholarship Recipient, 2007-2009

PUBLICATIONS

Heins SE, Wozniak AW, Colantuoni E, Sepulveda KA, Mendez-Tellez PA, Dennison-Himmelfarb C, Needham DM, Dinglas VD. Factors associated with missed assessments in a 2-year longitudinal study of acute respiratory distress syndrome survivors. (2018). In Press. *BMC Medical Research Methodology.*

Heins SE, Sorbero MJ, Jones CM, Dick AW, Stein BD. High-risk Prescribing to Medicaid-Enrollees Receiving Opioid Analgesics: Individual and County Level Factors. (2018). *Substance Use and Misuse.*

Heins SE, Crifasi CK. Distinctive injury deaths: The role of environment, policy, and measurement across states. (2016). *Injury Prevention* 22(4): 247-252.

Roberts ET, DuGoff EH, **Heins SE**, Swedler DI, Castillo RC, Feldman DR, Wegener ST, Canudas-Romo V, Anderson GF. Evaluating Clinical Practice Guidelines Based on Their Association with Return to Work in Administrative Claims Data. (2015) *Health Services Research*. 51(3): 953-987.

Heins SE, Feldman DR, Bodycombe D, Wegener ST, Castillo RC. Early opioid prescription and risk of long-term opioid use among US workers with back and shoulder injuries: a retrospective cohort study. (2015). *Injury Prevention*. 22(3): 211-215.

Archer KR., **Heins SE**, Abraham CM, Obremskey WT, Wegener ST, Castillo RC. Clinical Significance of Pain at Hospital Discharge Following Traumatic Orthopaedic Injury: General Health, Depression, and PTSD Outcomes at 1 Year. (2015). *Clinical Journal of Pain* 32(3): 196-202.

Wegener ST, Castillo RC, **Heins SE**, Bradford AN, Newell MZ, Pollak AN, MacKenzie EJ. Development and validation of the Readiness to Engage in Self-Management after Traumatic Injury Questionnaire. (2014). *Journal of Rehabilitation Psychology* 59(2): 203.

Trujillo AJ, **Heins SE**, Anderson GF, Castillo RC. Geographic variability of adherence to occupational injury treatment guidelines. (2014). *Journal of Occupational and Environmental Medicine*, *56*(12), 1308-1312.

Castillo RC, Wegener ST, **Heins SE**, Haythornthwaite JA, MacKenzie EJ, Bosse MJ, and the LEAP Study Group. Longitudinal relationships between anxiety, depression, and pain: Results from a two-year cohort study of trauma patients. (2013). *Pain* 154(12): 2860-2866.

Heins SE, Feldman DF, DuGoff EF, Wegener ST, Castillo RC. Development and validation of a categorization methodology for occupational back and shoulder injuries. (2013) *Health Services Outcomes and Research Methodology*, 13(2-4):140-156.

Castillo RC, Wegener ST, Newell MZ, Carlini AR, Bradford AN, **Heins SE**, Pollak AN, Teter H, MacKenzie EJ. Early evaluation of the Trauma Survivors Network at a major Level I trauma center. (2013) *Journal of Trauma and Acute Care Surgery* 74(6): 1534-1540.

Bradford AN, Castillo RC, Carlini AR, Wegener ST, Frattaroli S, **Heins SE,** MacKenzie EJ. Barriers to implementation of a hospital-based program for survivors of traumatic injury. (2013) *Journal of Trauma Nursing* 20(2): 89-99.

Roberts ET, DuGoff EH, Castillo RC, **Heins SE**, Anderson GF. A Decomposition analysis of medical expenditure growth among injured workers. (2012). *Journal of Healthcare Finance.* 40 (2): 59-74.

CONFERENCE POSTERS AND PRESENTATIONS

Heins SE, Castillo RC. Reducing Prescription Opioid Mortality: State-Level Morphine Equivalent Daily Dose Policies, 2007-2017. (2017). Poster presentation at the American Public Health Association annual meeting, Atlanta, GA.

Heins SE, Castillo RC. Evaluating the impact of state workers' compensation guidelines on opioid prescribing practices. (2017). Poster and Podium presentations at International Society for Pharmacoeconomics and Outcomes Research, Boston, MA.

Castillo RC, Carlini AR, **Heins SE**, Jarman MP. Short and long-term opioid utilization in a large dataset of occupational injury patients. (2016). Poster presentation at Academy Health Annual Meeting, Boston, MA.

Heins SE, Gudzune KA, Lemke KW, Lasser E, Kharrazi H, Richards TM, Weiner JP. Using Body Mass Index from Electronic Health Records to improve claims-based risk adjustment. (2016). Poster Presentation at The ACG System Conference, San Diego, CA.

Heins SE, Feldman DR, Bodycombe D, Wegener ST, Castillo RC. Early opioid prescription and risk of long-term opioid use among US workers with back and shoulder injuries: a retrospective,

longitudinal cohort study. (2015). Podium presentation at the Society for Advancement of Violence and Injury Research meeting, New Orleans, LA.

Castillo RC, Wegener ST, **Heins SE**, Abraham C, Obremskey WR, Archer KR. The Course of Hospital Pain Following Orthopaedic Trauma Surgery. (2014). Poster presentation at the American Pain Society Annual Meeting, Tampa, FL.

Archer KR, Castillo RC, **Heins SE**, Abraham CM, Obremskey WT, Wegener ST. Impact of early postoperative pain on outcomes one year following traumatic orthopaedic injury. (2013). Podium presentation at the Orthopedic Trauma Association Annual Meeting, Phoenix, AZ.

Heins SE, Feldman DR, DuGoff EH, Wegener ST, Castillo RC. Development and evaluation of a categorization methodology for occupational back and shoulder injuries. (2013). Poster presentation at Academy Health Annual Meeting, Baltimore, MD.

Roberts ET, DuGoff EH, Canudas-Romo V, **Heins SE**, Swedler D, Feldman DR, Wegner ST, Castillo RC. Measuring the Association between Clinical Practice Guidelines and Return to Work using Administrative Claims Data. (2013). Poster presentation at Academy Health Annual Meeting, Baltimore, MD.

Castillo RC, **Heins SE**, Feldman DF, Roberts E, Wu A, Simmons M, Medford A, Trujillo A. Development and cost implications of quality of care indicators for shoulder and back injuries. (2013). Poster presentation at Academy Health Annual Meeting, Baltimore, MD.

Mroz TM, Carlini AR, Archer KR, Wegener ST, Hoolachan JI, Stiers W, **Heins SE**, Castillo RC. A predictive model for high medical and indemnity costs following occupational injuries. (2013). Poster presentation at Academy Health Annual Meeting, Baltimore, MD.

Castillo RC, Wegener ST, **Heins SE**, Haythornthwaite JA, MacKenzie EJ, Bosse MJ, and the LEAP Study Group. Anxiety and depression in the etiology of chronic pain: Results from a two-year cohort study of trauma patients. (2013). Poster presentation at the National Meeting for the Safe States Alliance and the Society for Advancement of Violence and Injury Research, Baltimore, MD.

Castillo RC, Knutsen E, Belin E, **Heins SE**, Paryavi E. Validity of the Patient Satisfaction Questionnaire-18 for orthopaedic trauma. (2013). Poster presentation at Academy of Orthopaedic Surgeons Annual Meeting, Chicago, IL.

Roberts ET, DuGoff EH, Castillo RC, **Heins SE**, Anderson GF. A decomposition analysis of medical expenditure growth among injured workers. (2012). Poster presentation at the American Public Health Association Annual Meeting, San Francisco, CA.

Castillo RC, Wegener ST, Newell MZ, Carlini AR, Bradford AN, **Heins SE**, Pollak AN, Teter, H, MacKenzie EJ. (2012). Early evaluation of the Trauma Survivors Network at a major Level I trauma center. Poster presentation at Orthopedic Trauma Association Annual Meeting, Minneapolis, MN.

Archer KA, Castillo RC, Abraham CM, **Heins SE**, Song Y,Wegener ST, Obremskey WT. (2012). Development of a multidimensional postoperative pain tool for orthopedic trauma surgery. Poster presentation at Orthopedic Trauma Association Annual Meeting, Minneapolis, MN.

Heins SE, Lewenstein BV. HIV/AIDS Prevention Advertisements in Vietnam: Health Communication and Health Communities. (2011). Poster presentation at the National Conference for Undergraduate Research, Ithaca, NY.